

FIG. 1

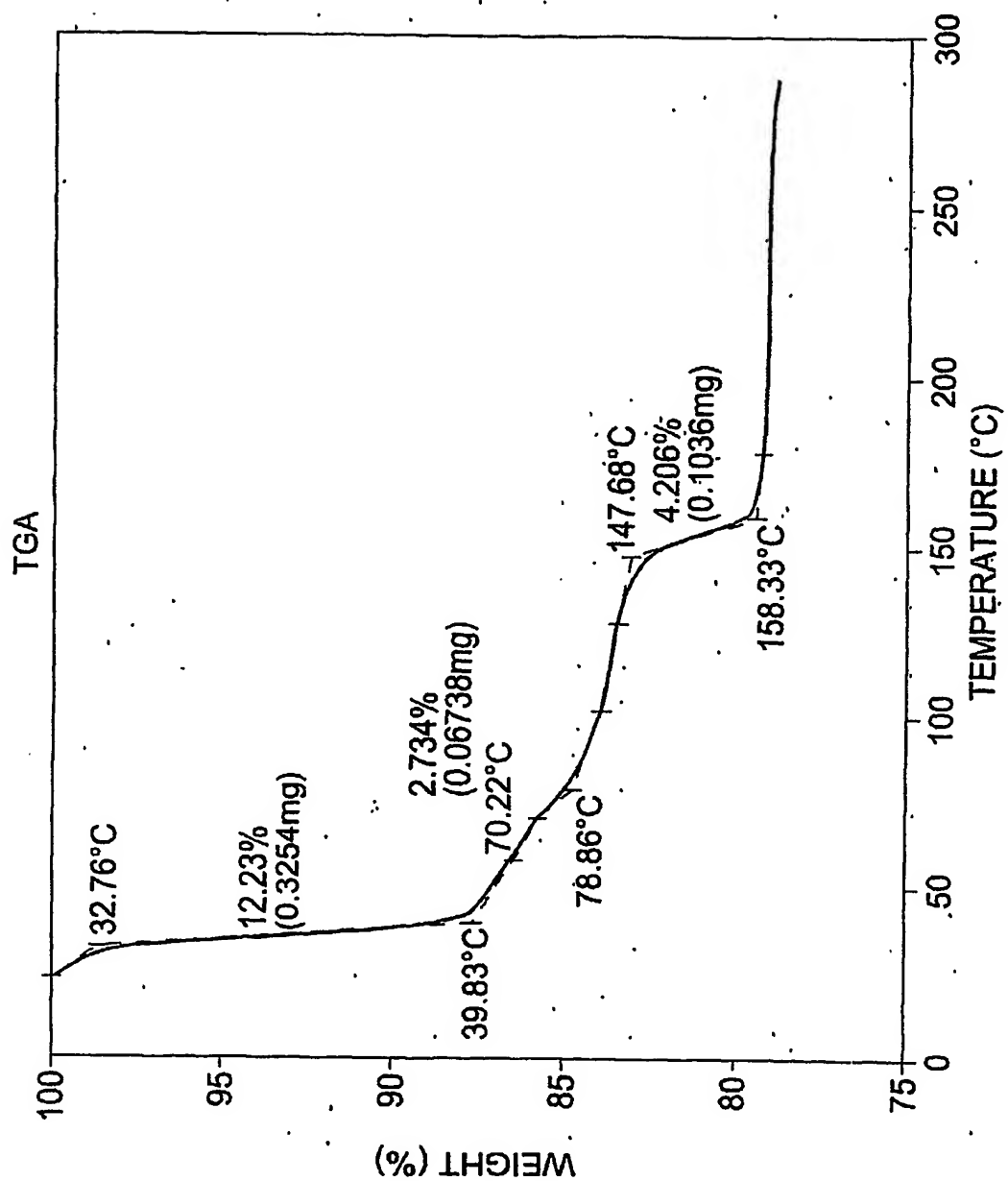


FIG. 2

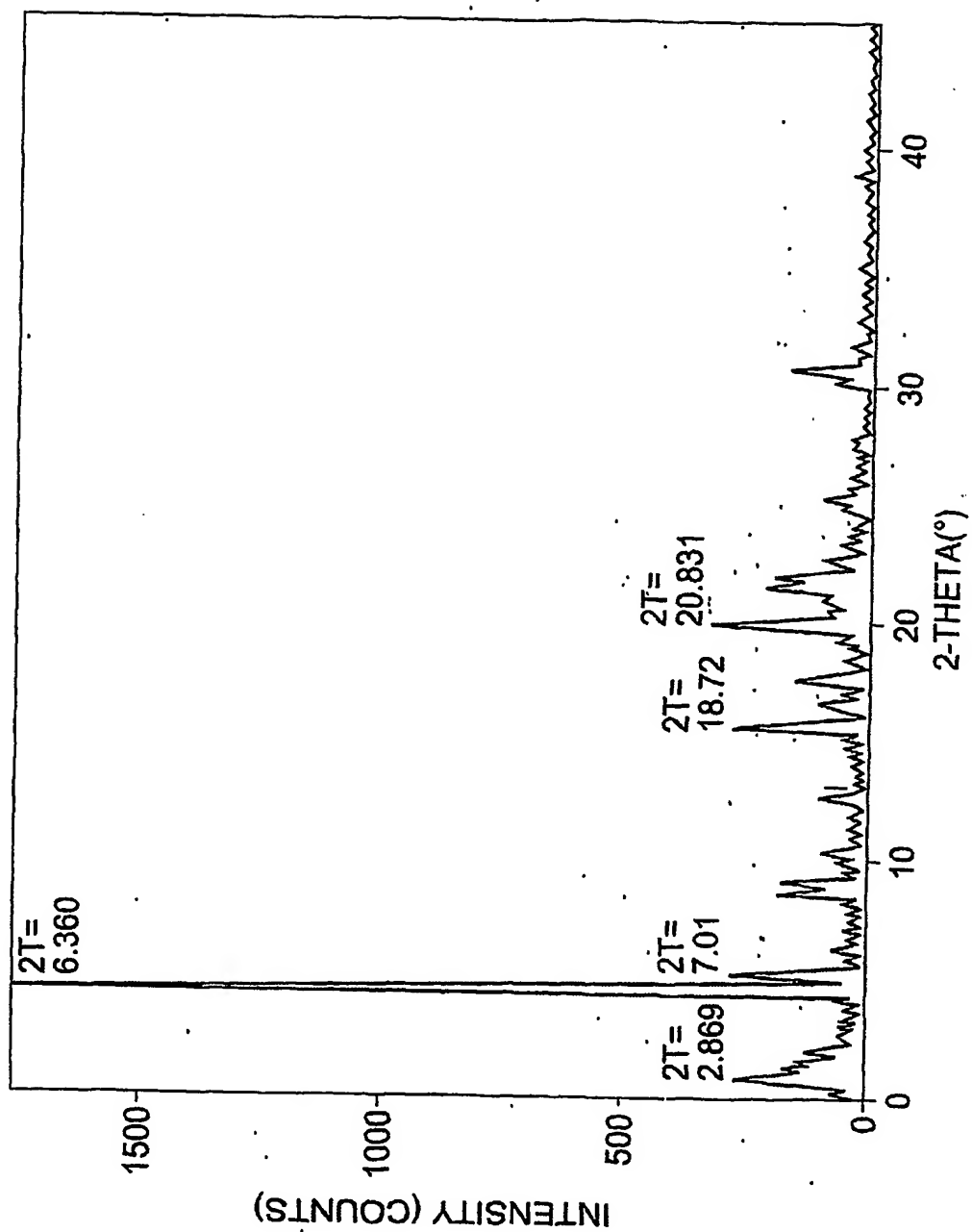


FIG. 3

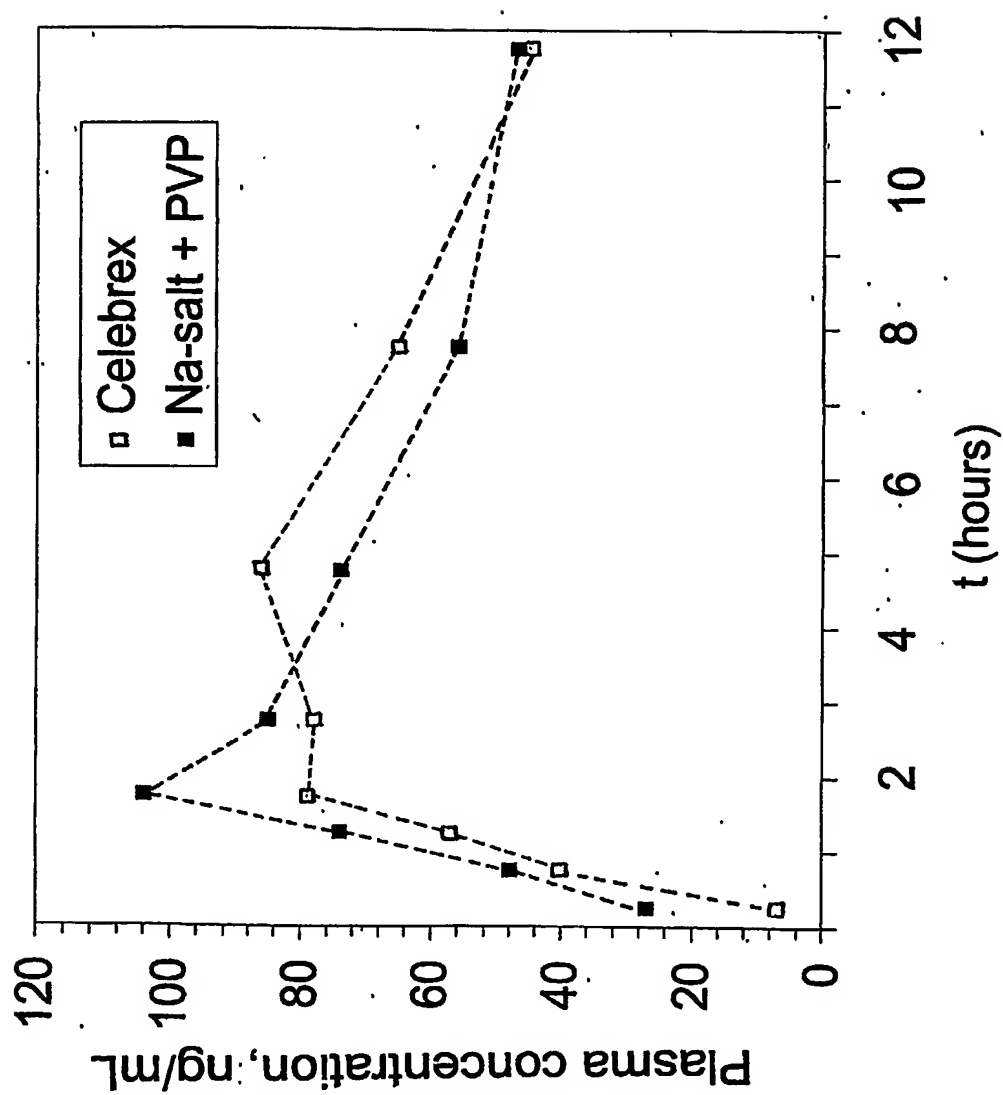


FIG. 4A

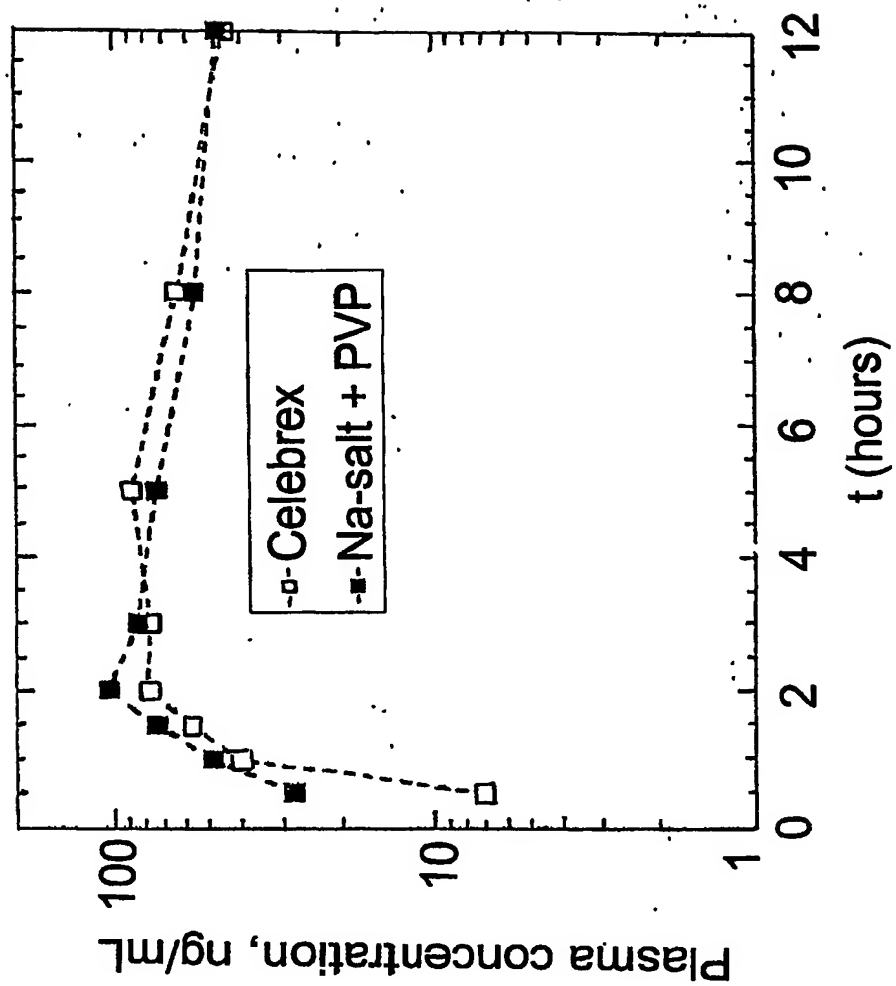


FIG. 4B

Formulation # & Dosing	TPI-336 Form	Percent Mass with respect to TPI-336 freeacid content					
		HPC	TPGS	Avicel	Pluronic F127	Pluronic L44	PEG400
1 – IV	Freeacid	--	--	--	--	--	--
2 – Oral	Freeacid	100	100	50	--	--	--
3 – Oral	Celebrex ( <i>i.e.</i> , freeacid)	--	--	--	--	--	--
4 – Oral	Na Hydrate	100	100	--	--	--	--
5 – Oral	Na Hydrate	100	100	50	--	--	--
6 – Oral	Na PG Solvate	100	100	--	--	--	--
7 – Oral	Na Hydrate	100	--	--	100	--	--
8 – Oral	Na Hydrate	100	--	--	100	40	--
9 – Oral	Na Hydrate	100	--	--	100	--	40

FIG. 5A

Formulation ID	Route	Mean dose (mg/kg)	C <sub>max</sub> (ng/mL)	T <sub>max</sub> (hr)	AUC(I) (ng•hr/mL)	t <sub>1/2</sub> (hr)	CL/F (mL/hr•kg)	F(%)
Celebrex <sup>a</sup>	Oral	5.09 (0.05)	654 (199)	1.25 (0.88)	7663 (3119)	9.3 (3.5)	798 (317)	40.5 (15.45)
Celecoxib <sup>a</sup>	IV	1.0 (0.00)	718 (91)	NA	3808 (933)	8.2 (2.9)	278 (77)	NA
Celecoxib free form/HPC/TPGS <sup>b</sup>	Oral	5.14 (0.124)	622 (484)	2.7 (1.5)	7290 (5624)	8.5 (2.0)	1072 (767)	29.80 (17.14)
Celecoxib Na/HPC/TPGS <sup>b</sup>	Oral	2.85 (0.27)	1635 (144)	0.4 (0.1)	10100 (4729)	7.7 (3.7)	281 (107)	103.2 (12.82)
Celecoxib Na/HPC/TPGS <sup>a</sup>	Oral	5.05 (0.12)	2495 (680)	0.75 (0.27)	17031 (4263)	9.0 (2.7)	311 (72)	89.15 (9.70)
Celecoxib Na/HPC/TPGS <sup>b</sup>	Oral	7.54 (0.24)	3445 (646)	0.80 (0.29)	24994 (7596)	7.1 (2.5)	318 (84)	99.43 (3.68)
Celecoxib Na PG/HPC/TPGS <sup>b</sup>	Oral	4.89 (0.49)	2955 (794)	0.8 (0.3)	22711 (4043)	7.7 (1.2)	225 (40.3)	109.4 (14.92)
Celecoxib Na/HPC/F127 <sup>c</sup>	Oral	5.29 (0.07)	2276 (272)	1.0 (0.0)	14669 (2496)	6.1 (2.9)	366 (67)	97.82 (3.36)
Celecoxib Na/HPC/F127/L44 <sup>c</sup>	Oral	5.26 (0.03)	3411 (529)	0.5 (0.0)	22365 (3448)	9.0 (1.8)	238 (38)	108.9 (2.57)
Celecoxib Na/HPC/F127/PEG400 <sup>c</sup>	Oral	5.45 (0.06)	3121 (119)	0.5 (0.0)	24377 (2469)	6.5 (3.2)	225 (25)	95.9 (0.68)

FIG. 5B

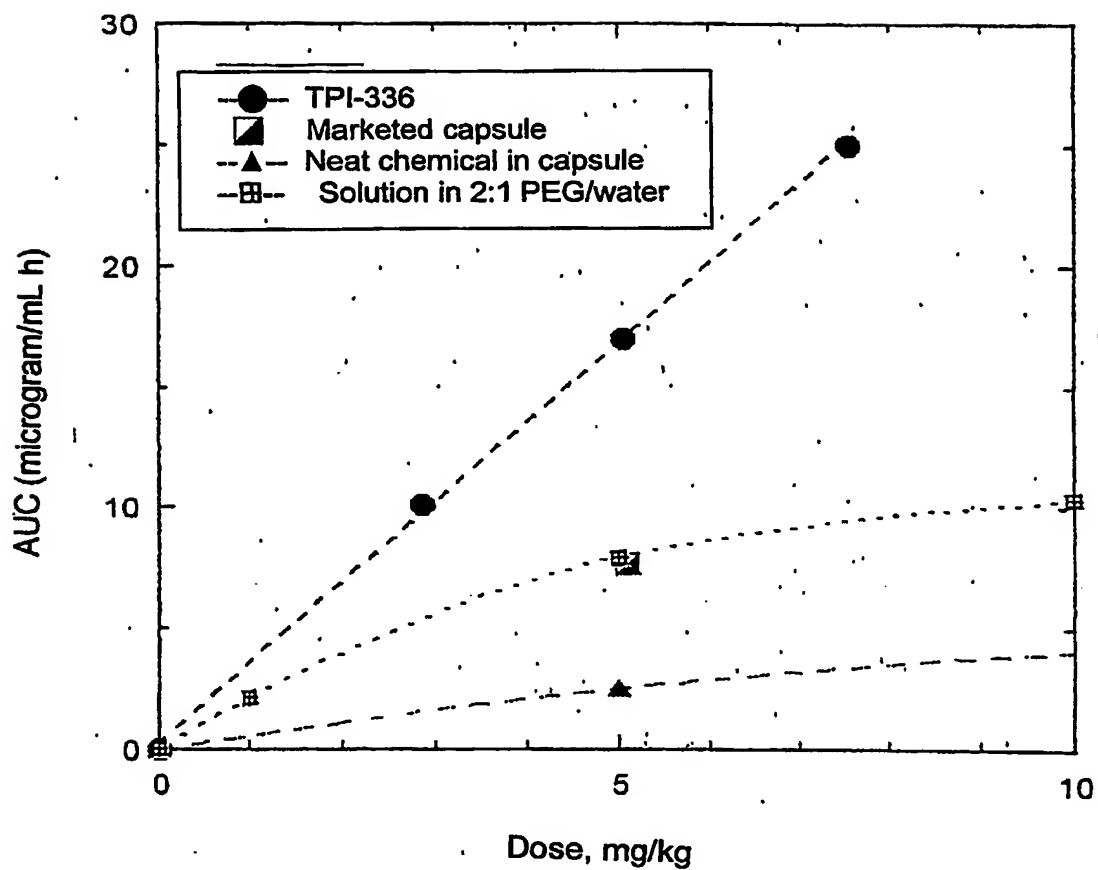


FIG. 5C



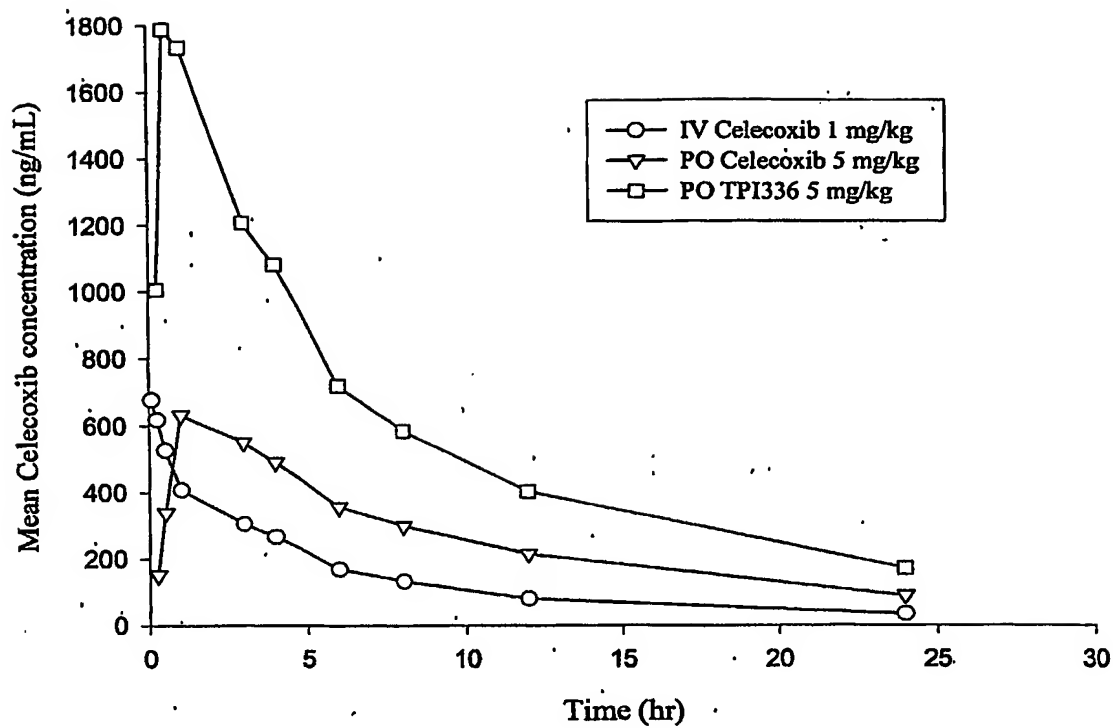
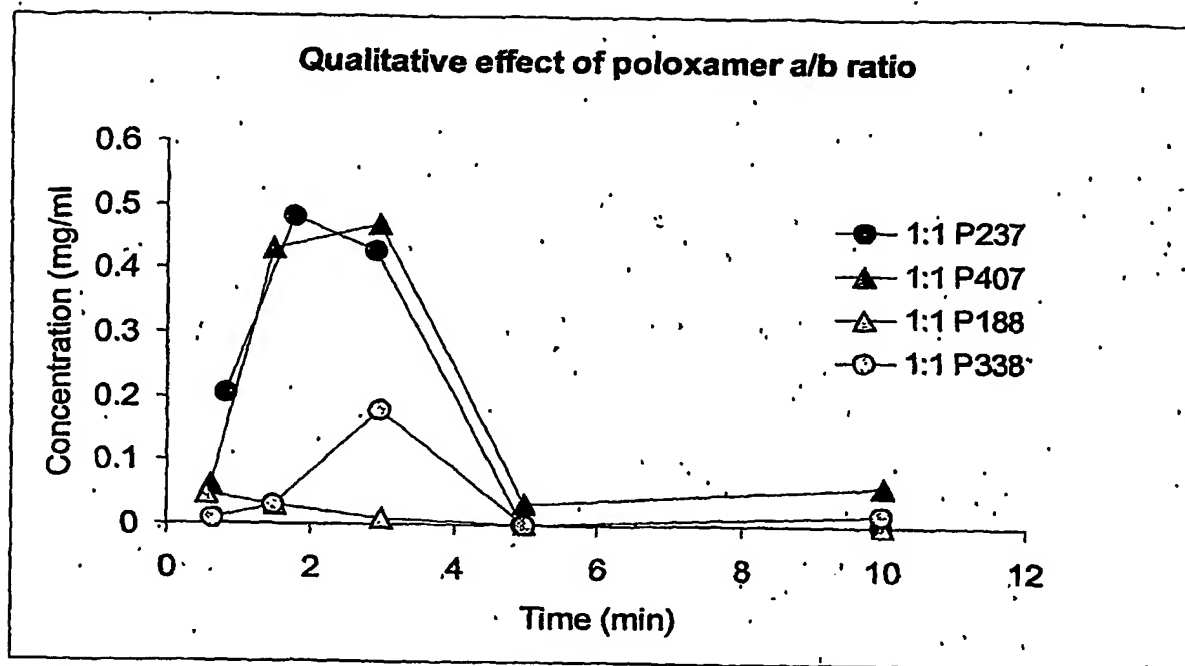


FIG. 6



Poloxamer	Physical form	a	b	Average molecular weight
124	Liquid	12	20	2090-2360
188	Solid	80	27	7680-9510
		64	37	6840-8830
338	Solid	141	44	12 700-17 400
		101	56	9840-14 600

Percent a	Percent b	Ratio a/b
0.38	0.63	0.60
0.75	0.25	2.96
		1.73
0.76	0.24	3.20
		1.80



FIG. 7

## Effects of Celluloses on Dissolution of 1/1 Vitamin E TPGS/TPI-336-Na at Room

Temperature

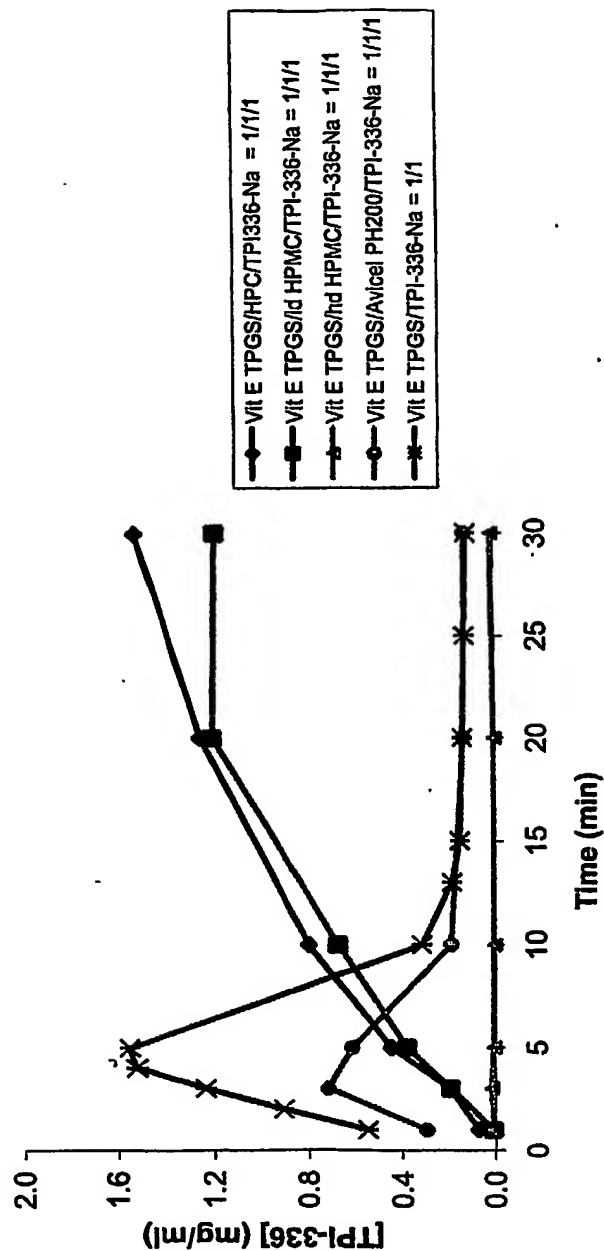


FIG. 8

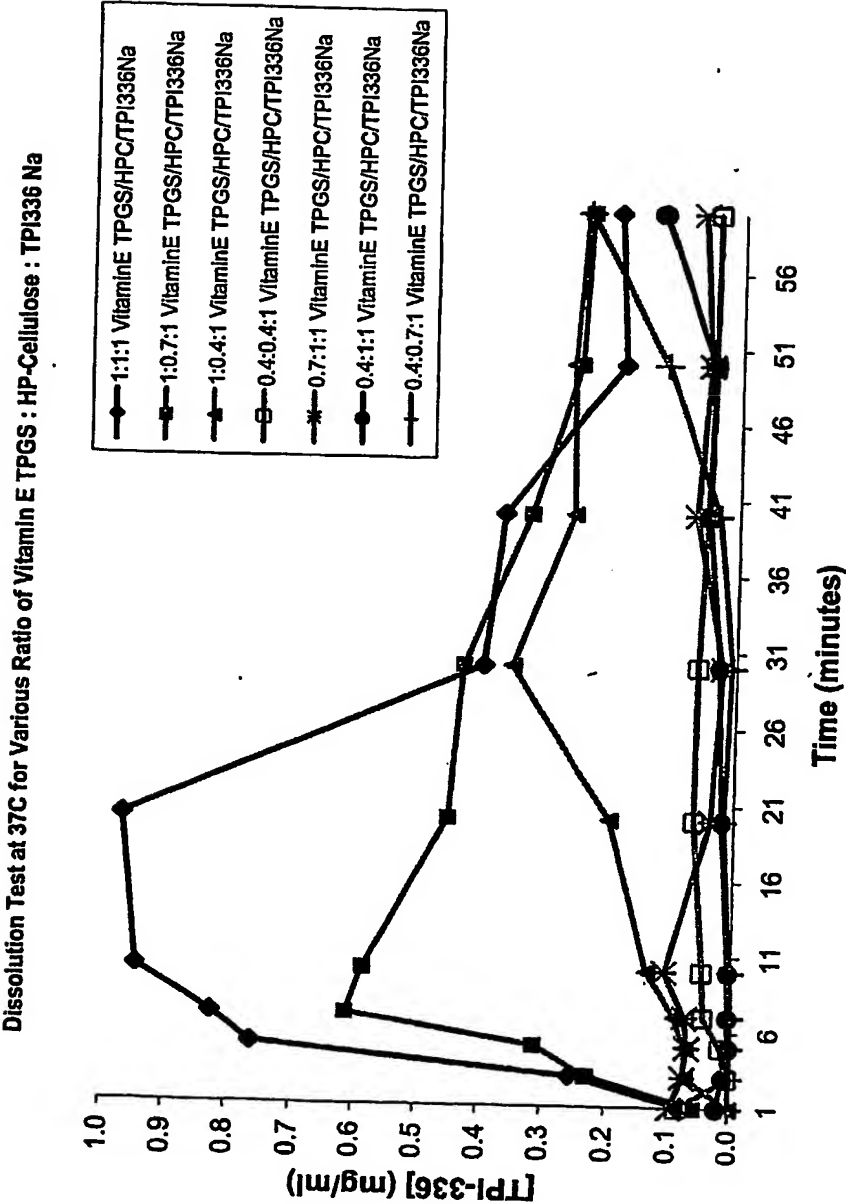


FIG. 9

Dissolution profile of TPI-336-Na in SGF from solid mixtures with  
excipients at room temperature

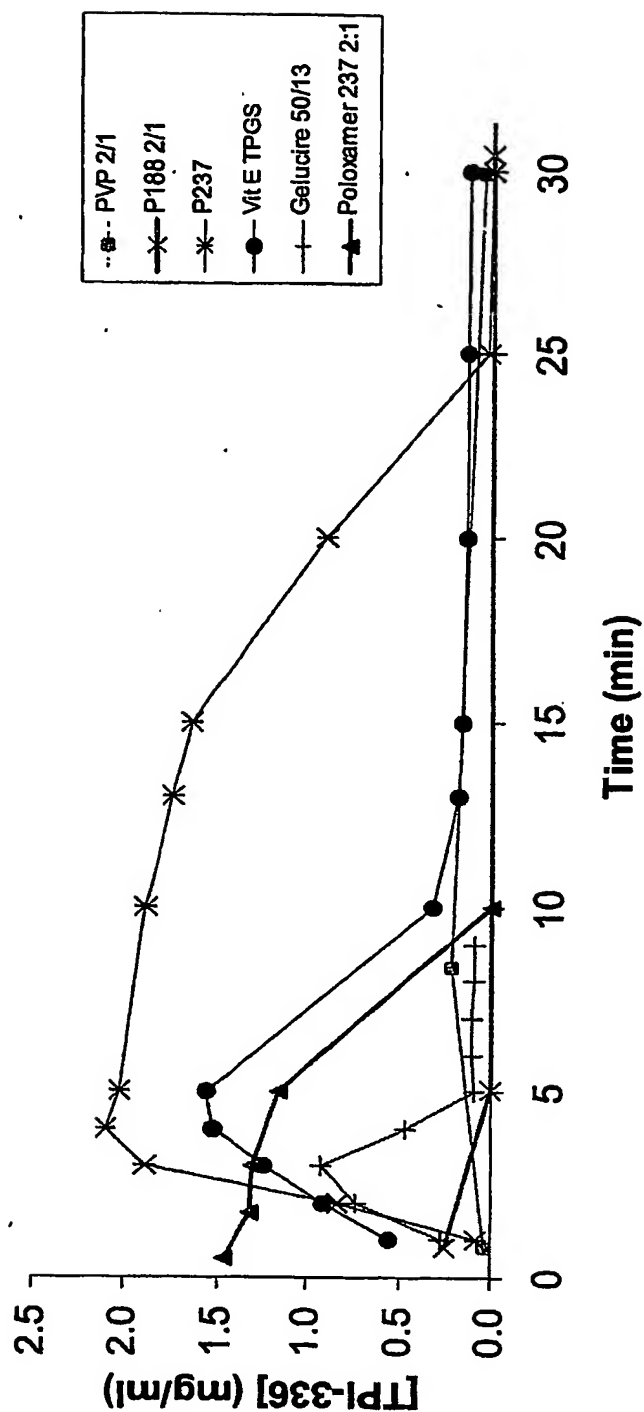


FIG. 10

Effect of Avicel and Silica Gel on the dissolution of TP1336Na/Vit E TPGS/HPC mixtures in SGF at 37C

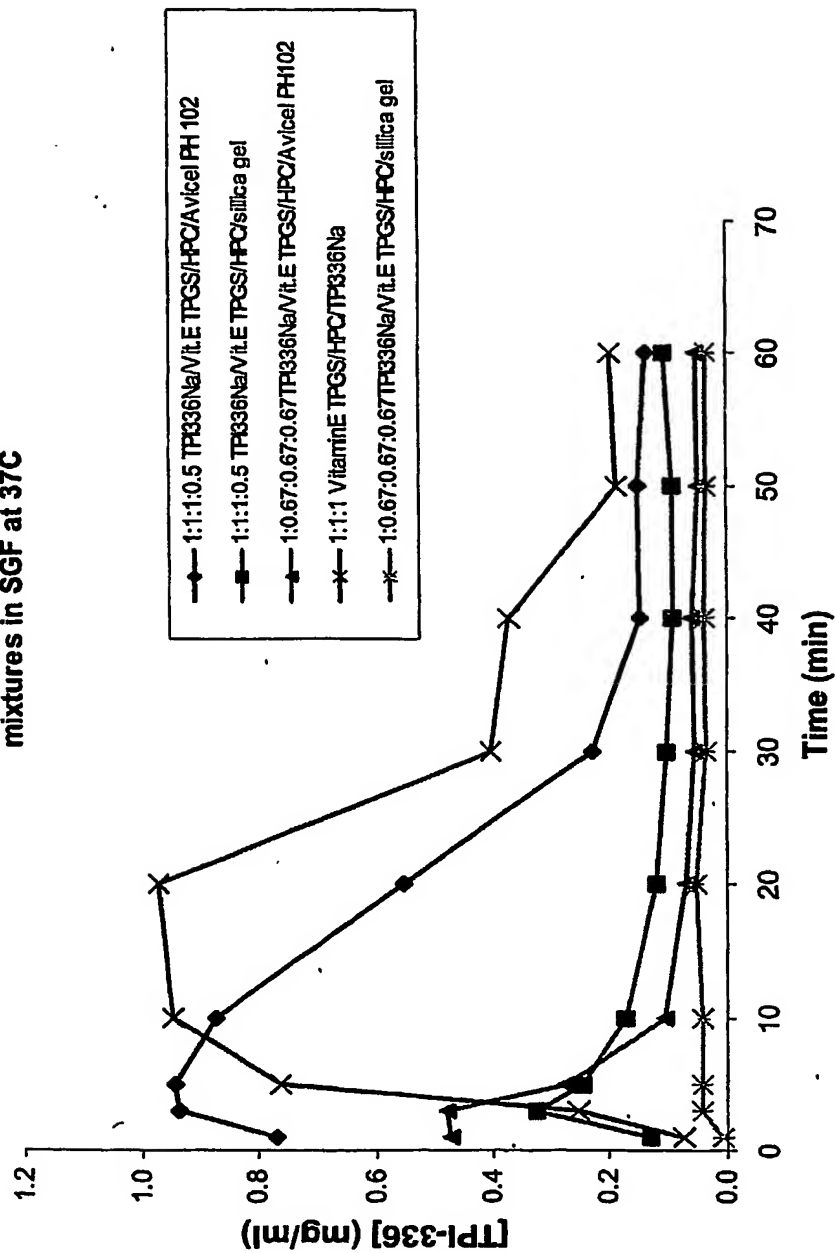


FIG. 11

Dissolution of TPI336Na at 37C in 5X diluted SGF

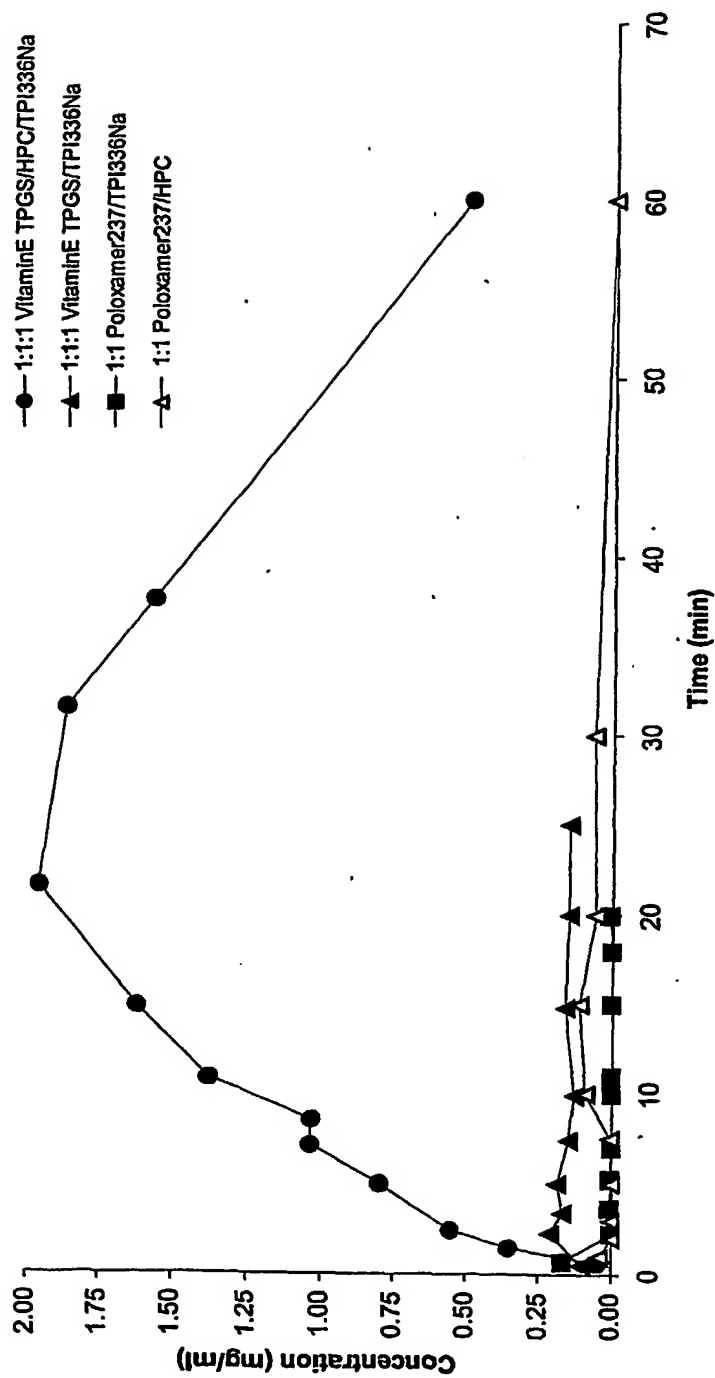


FIG. 12

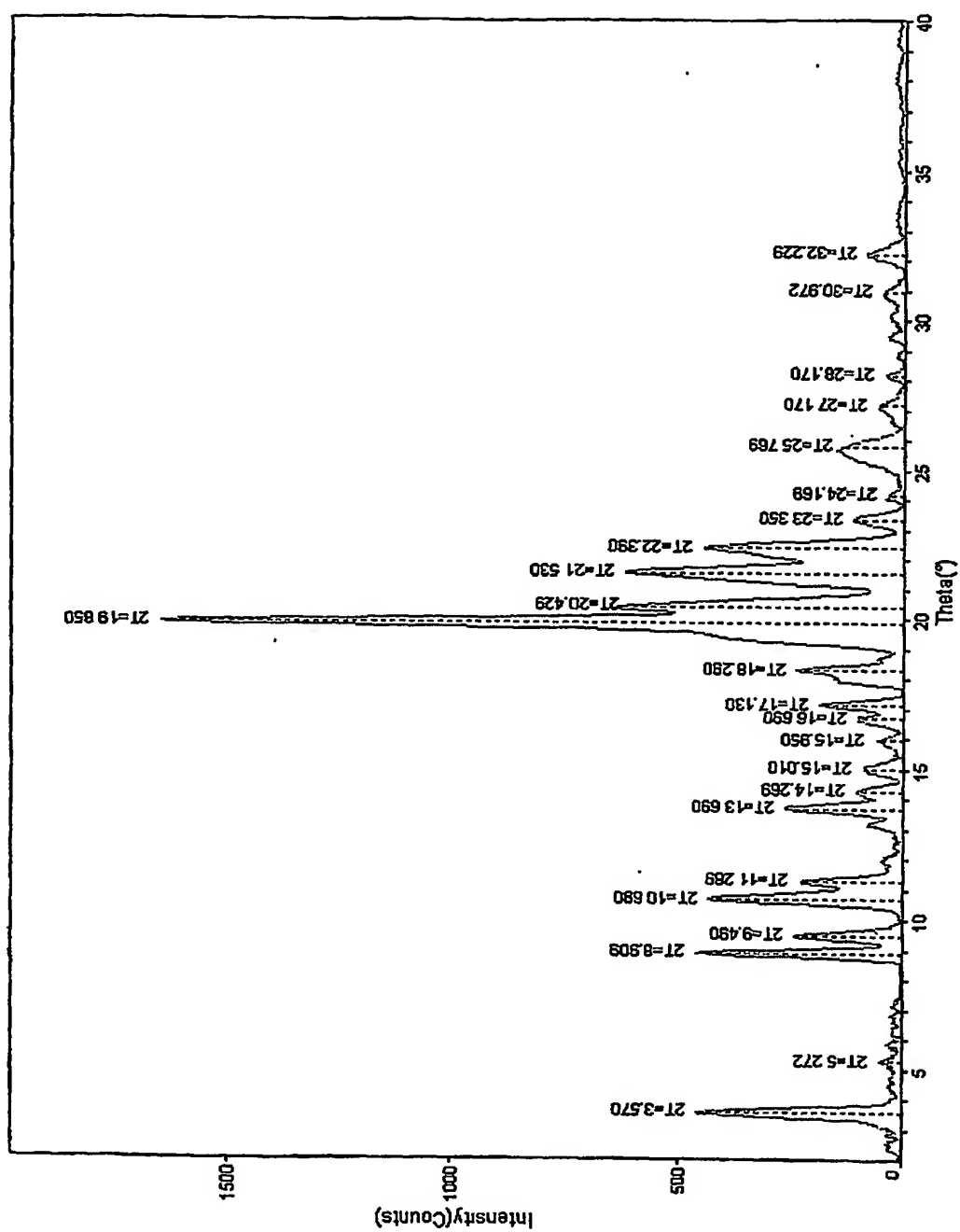


FIG. 13A



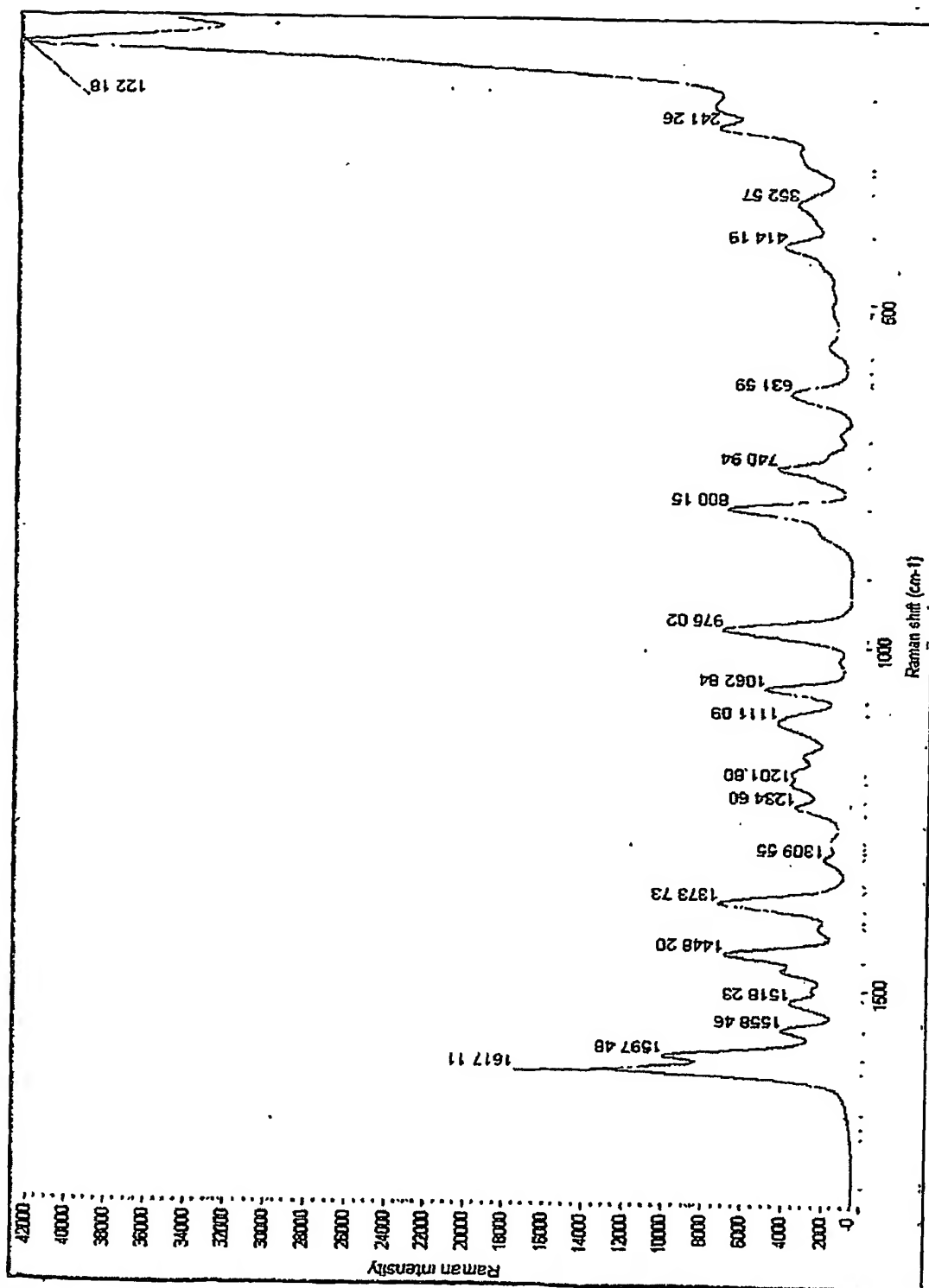


FIG. 13B

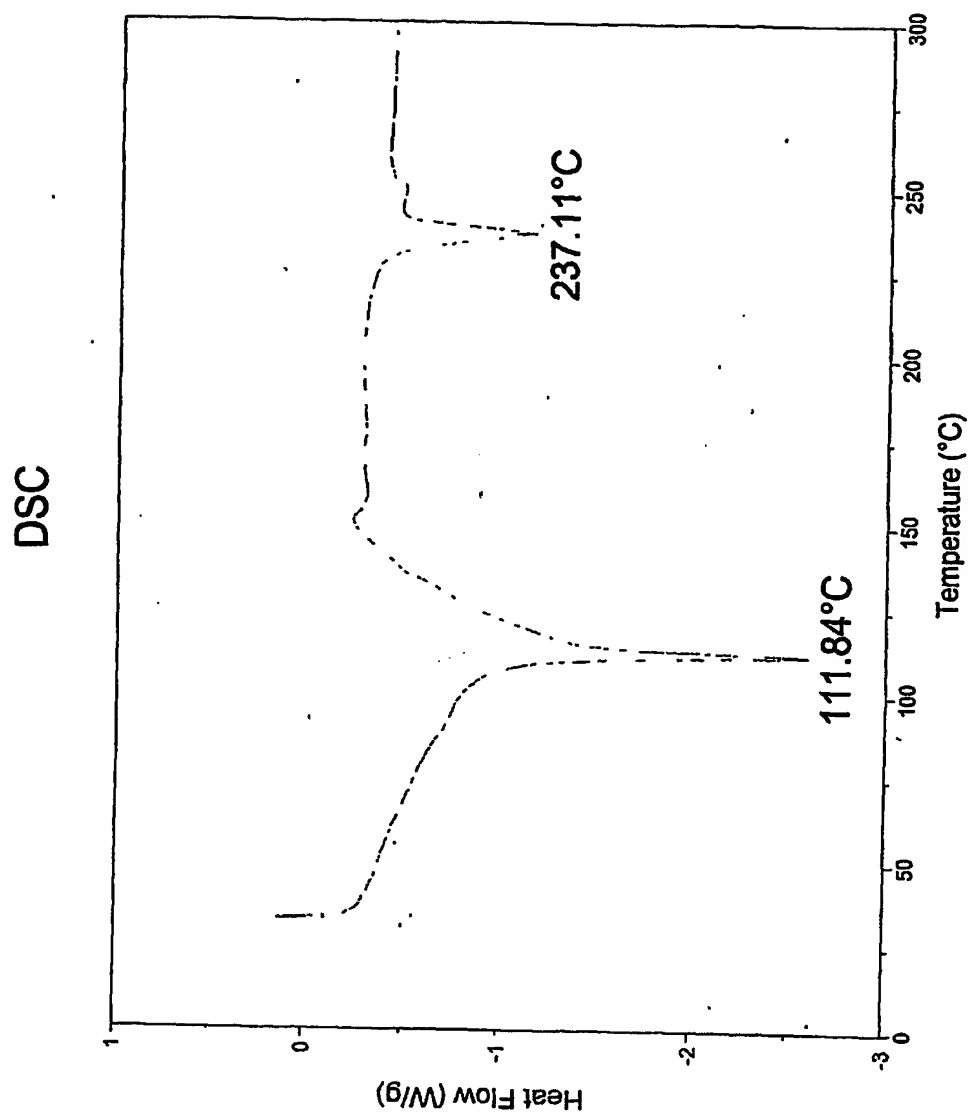


FIG. 14

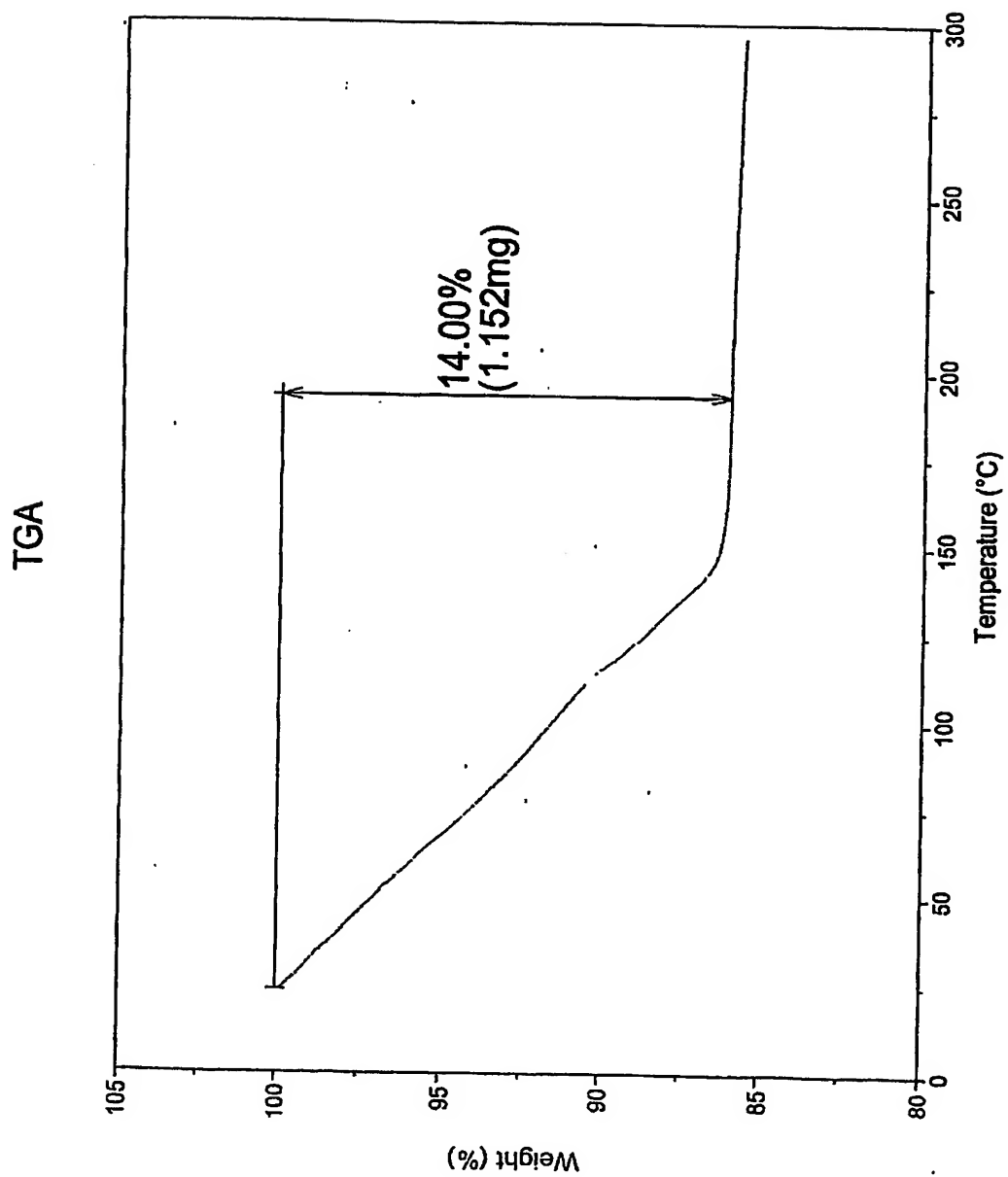


FIG. 15

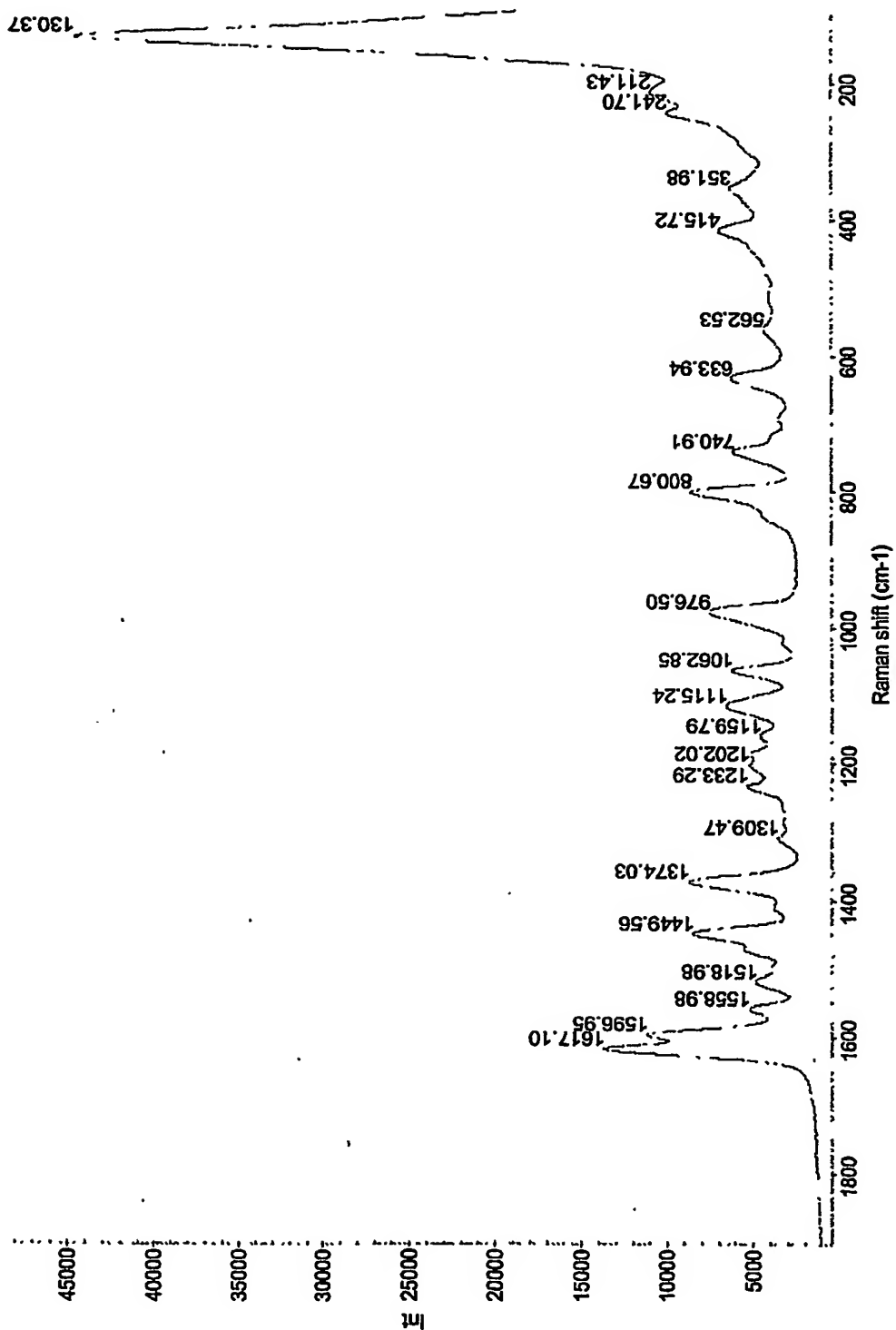


FIG. 16

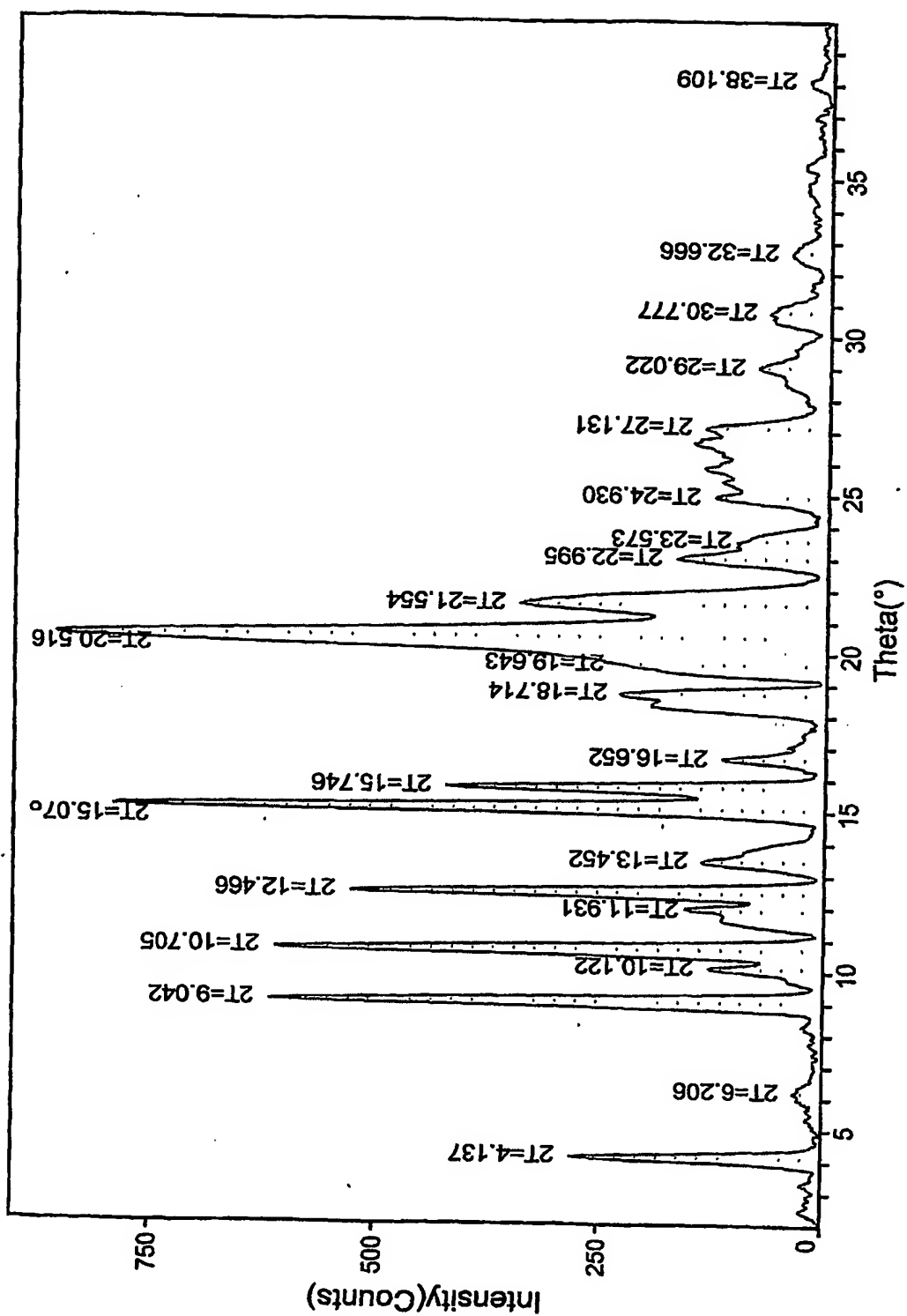


FIG. 17

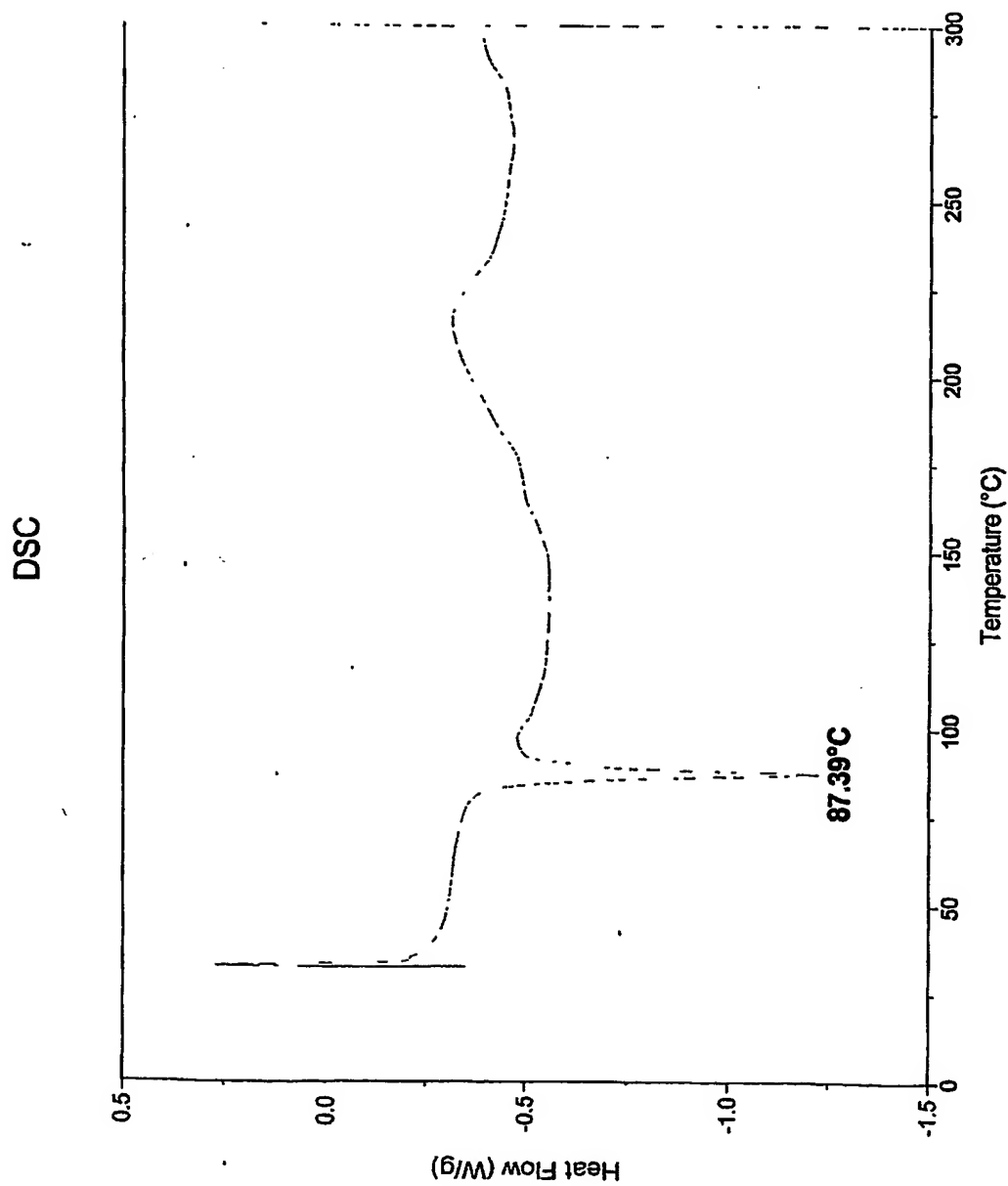


FIG. 18

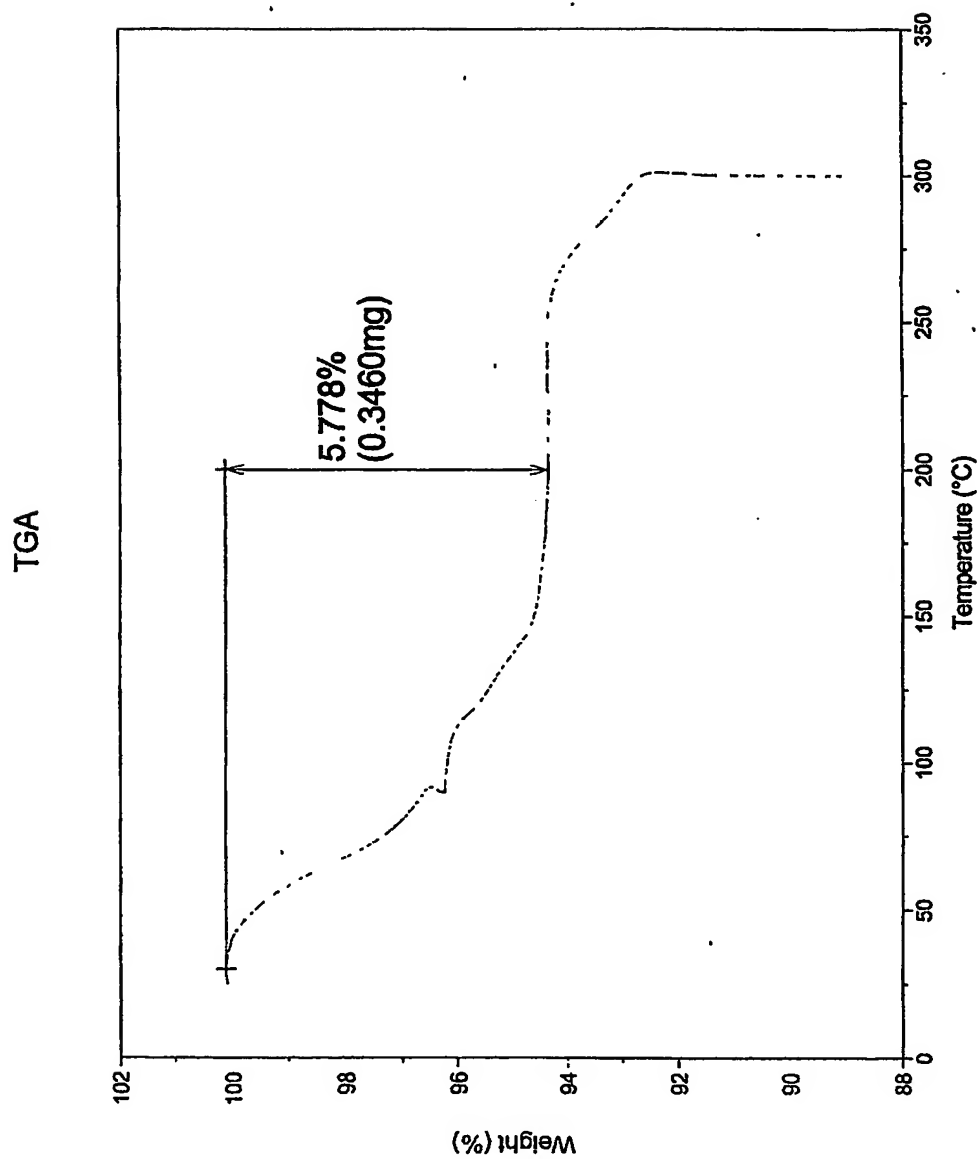


FIG. 19

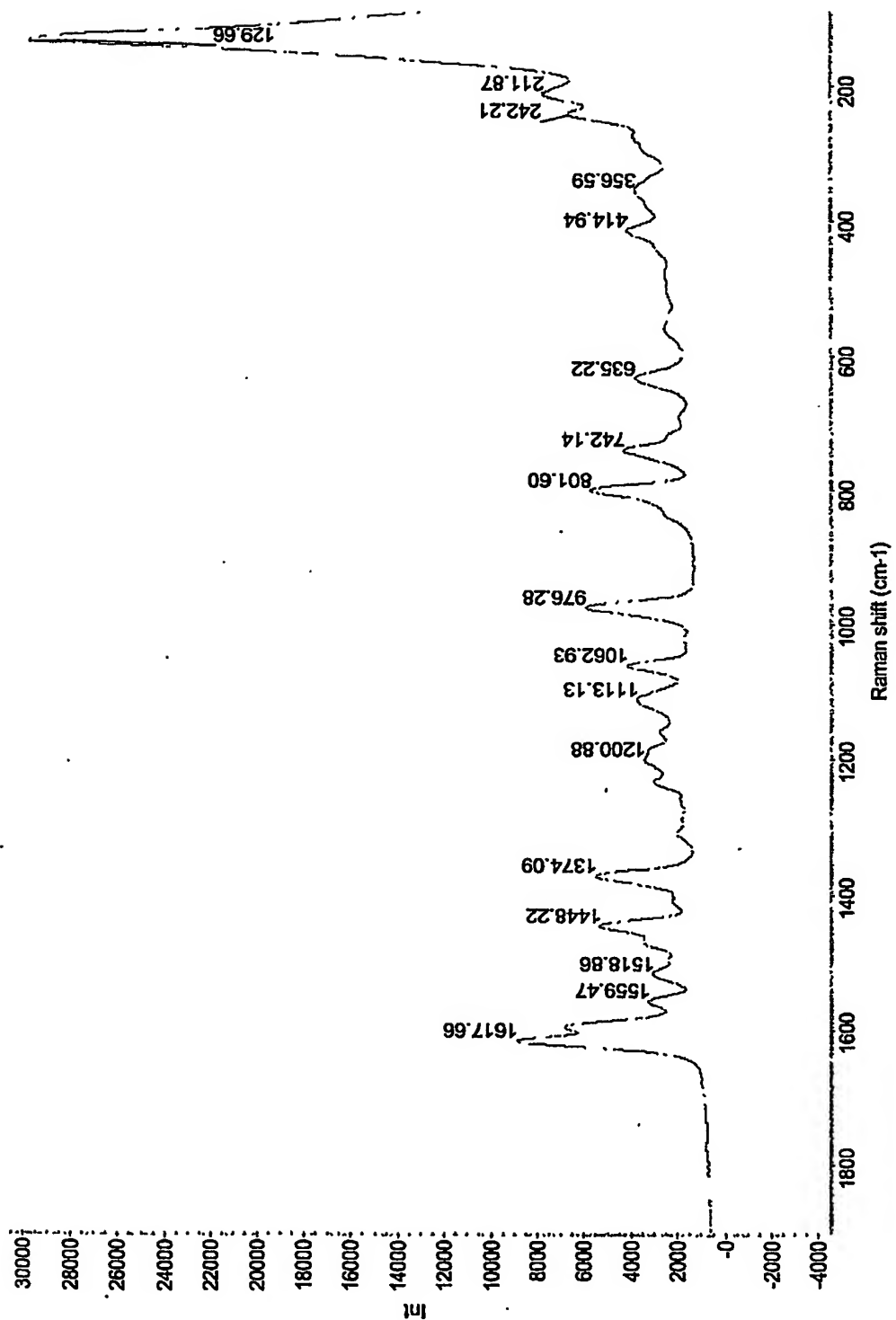


FIG. 20



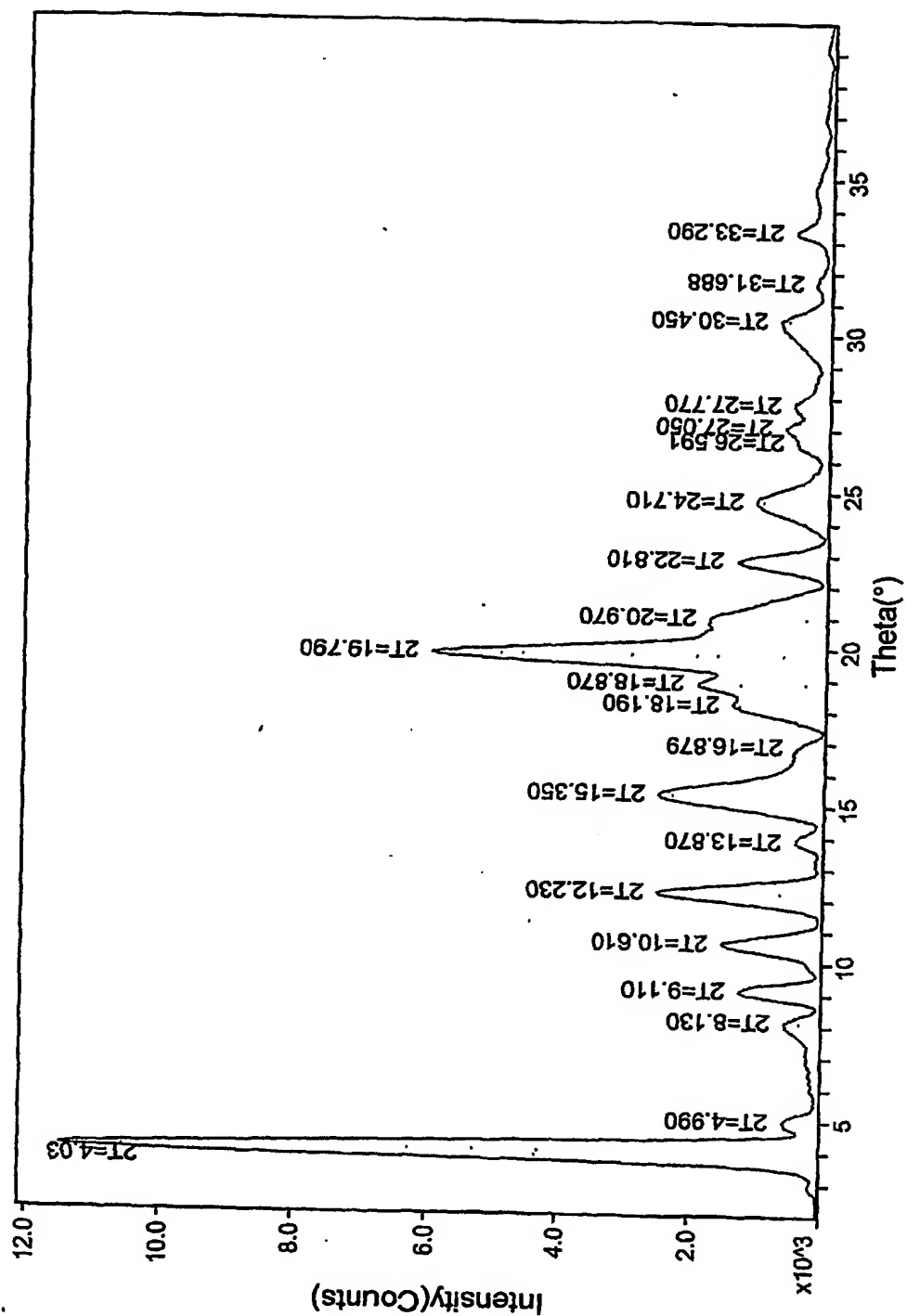


FIG. 21

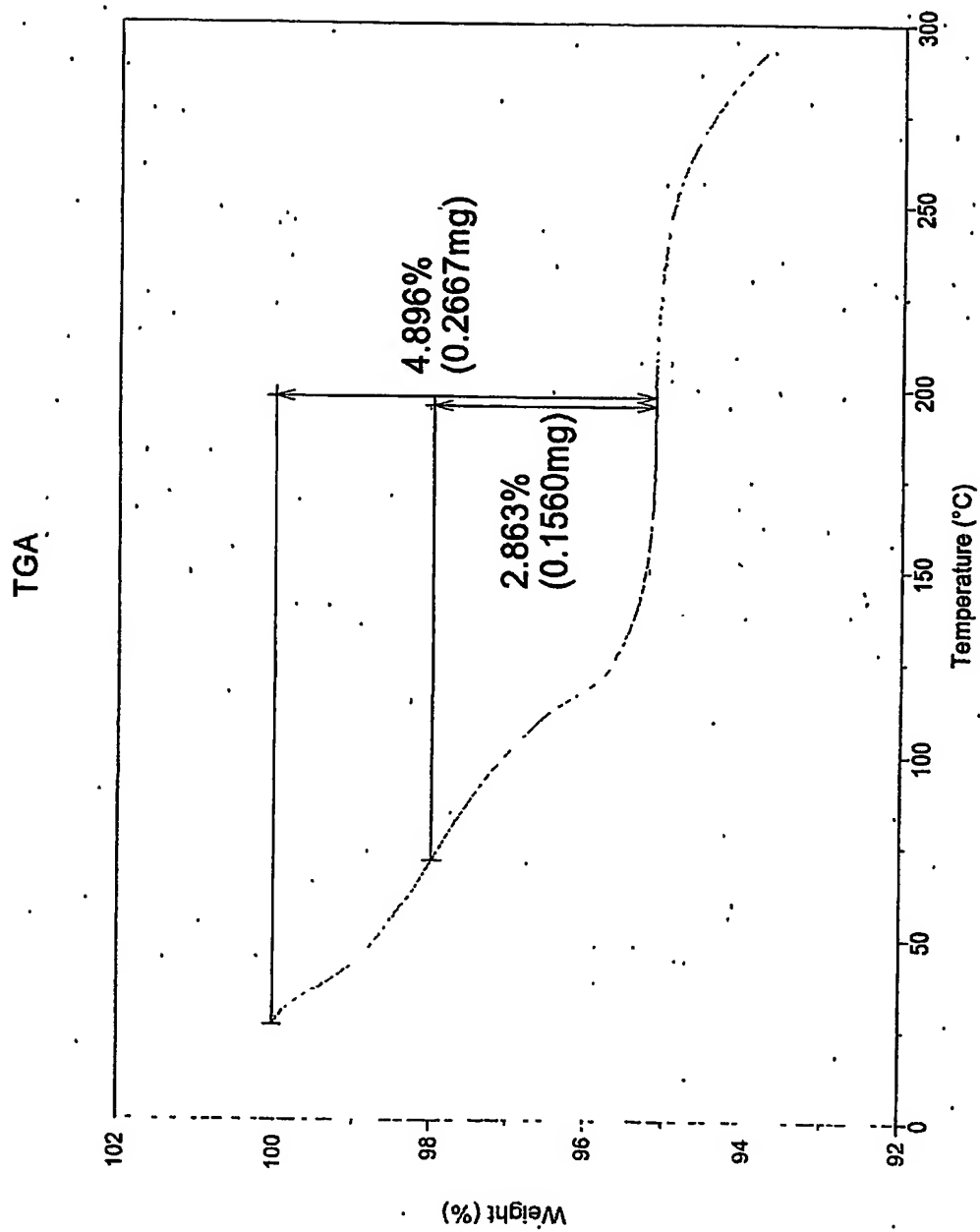


FIG. 22

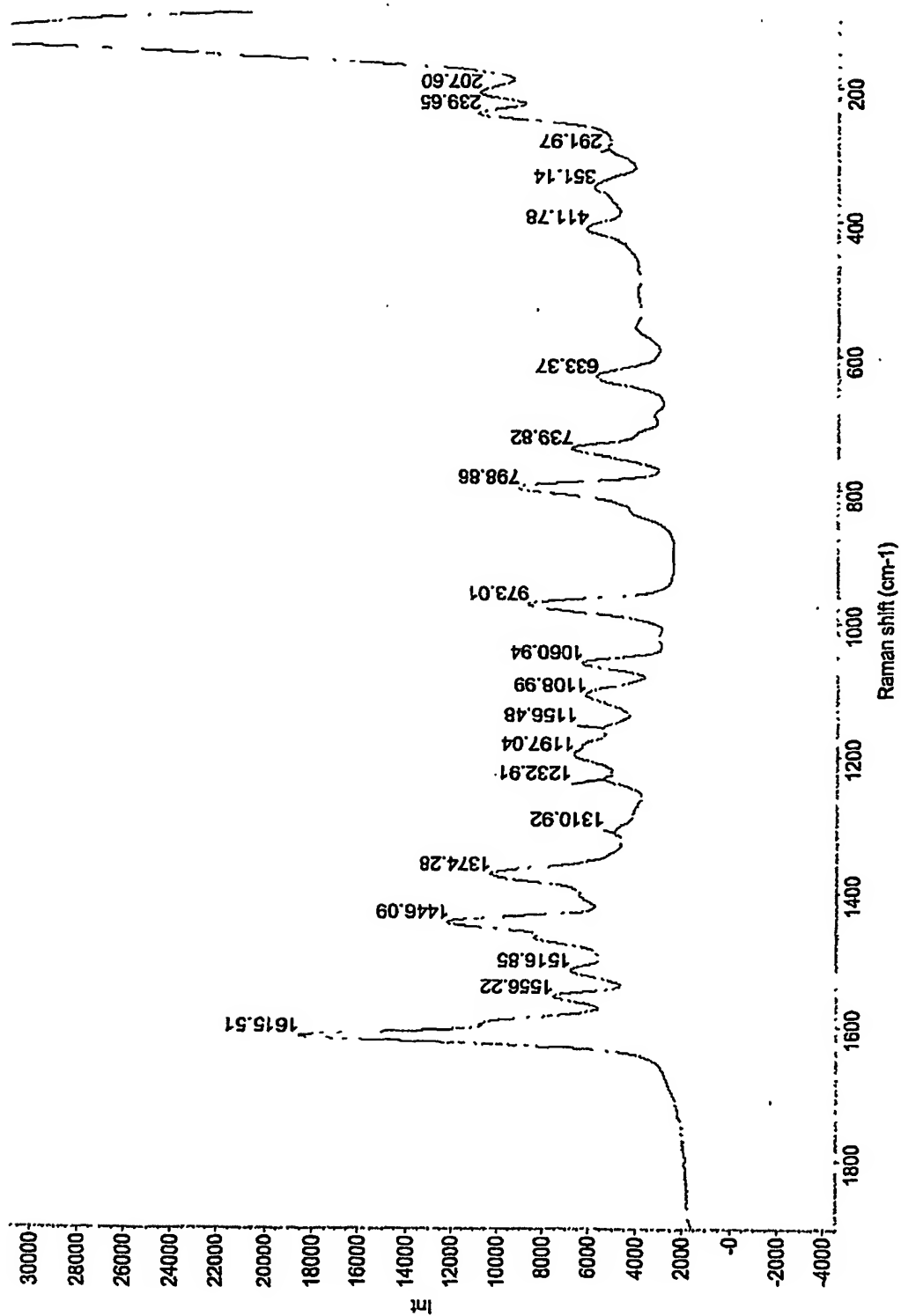


FIG. 23

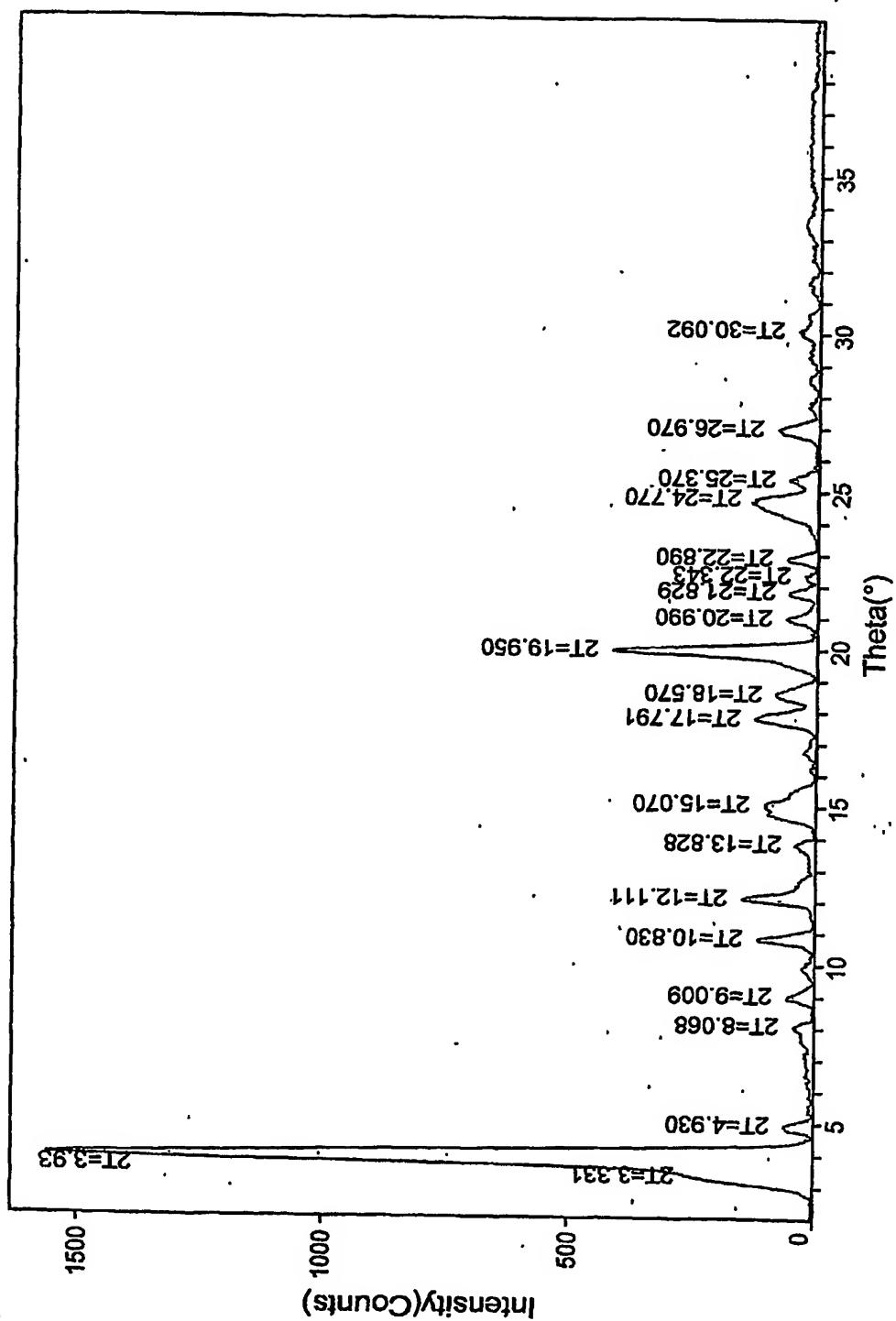


FIG. 24

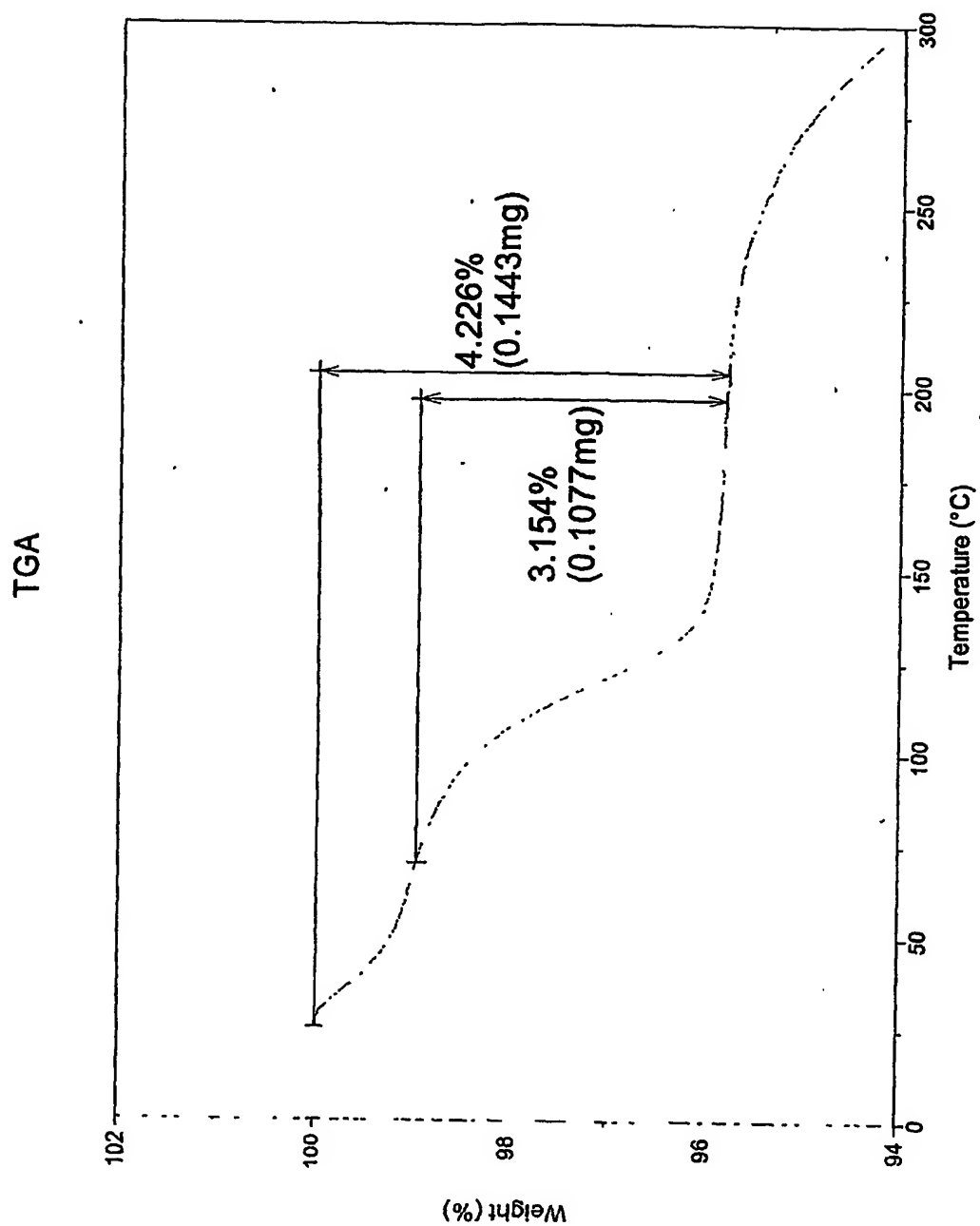


FIG. 25

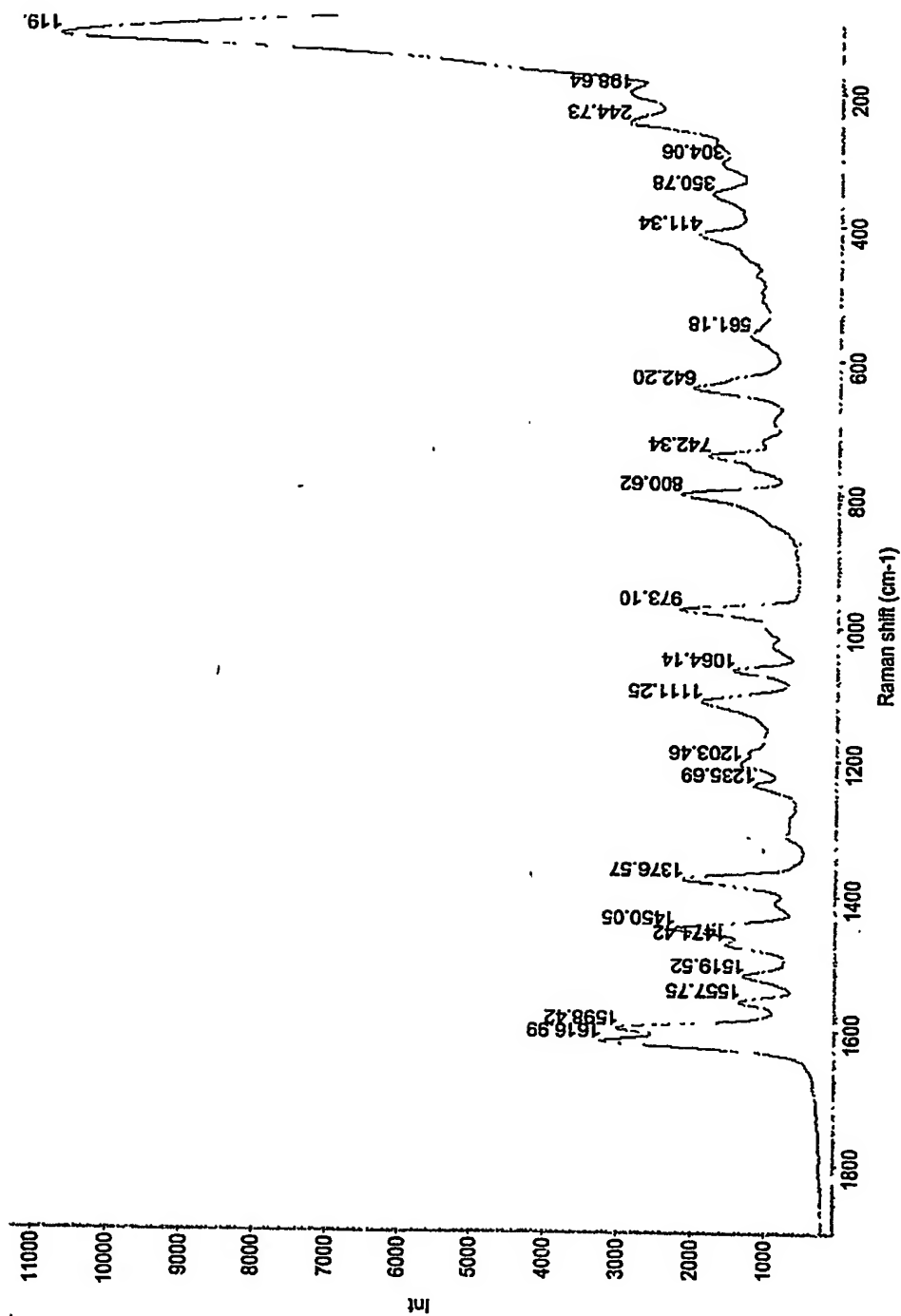


FIG. 26

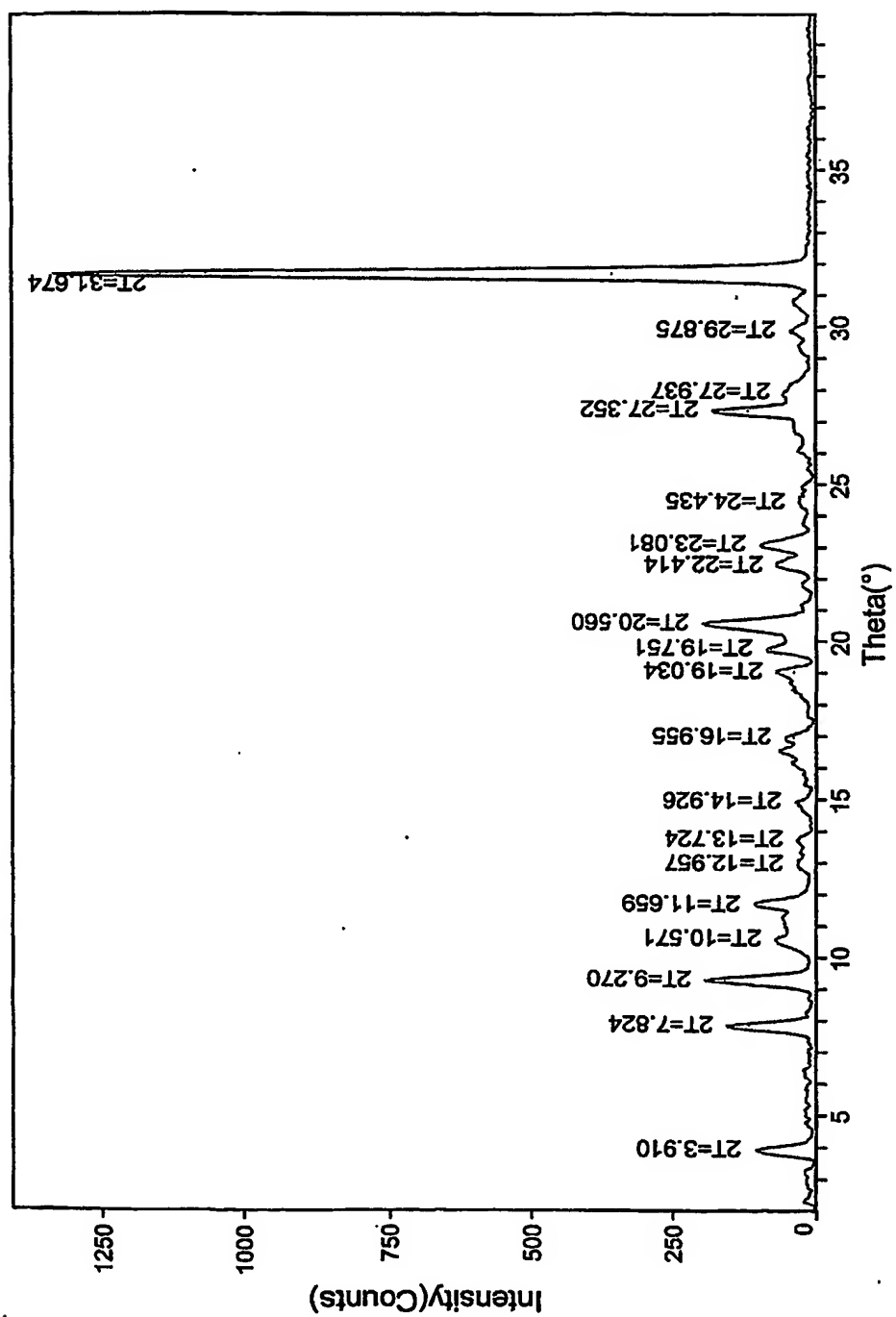


FIG. 27

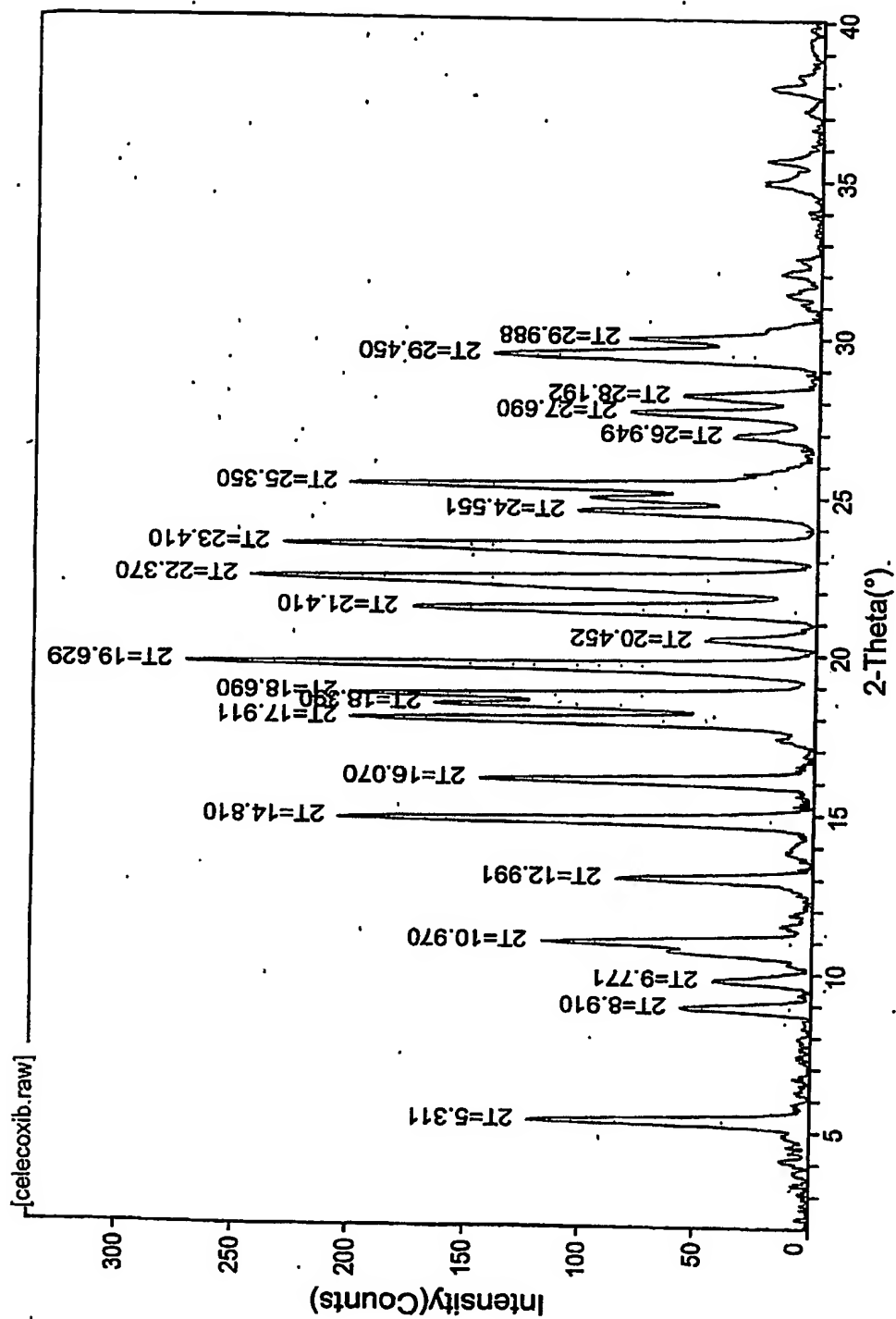


FIG. 28



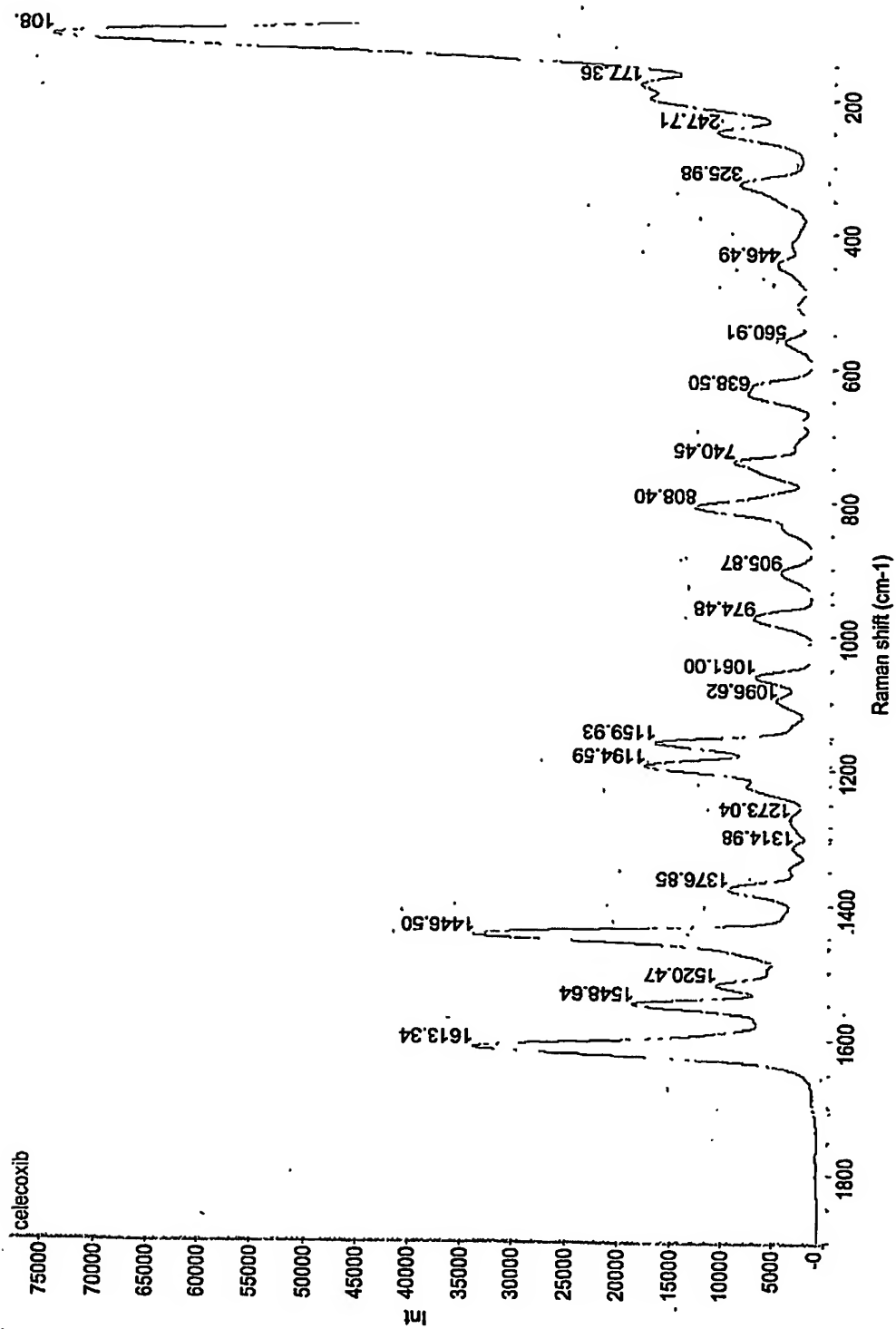


FIG. 29

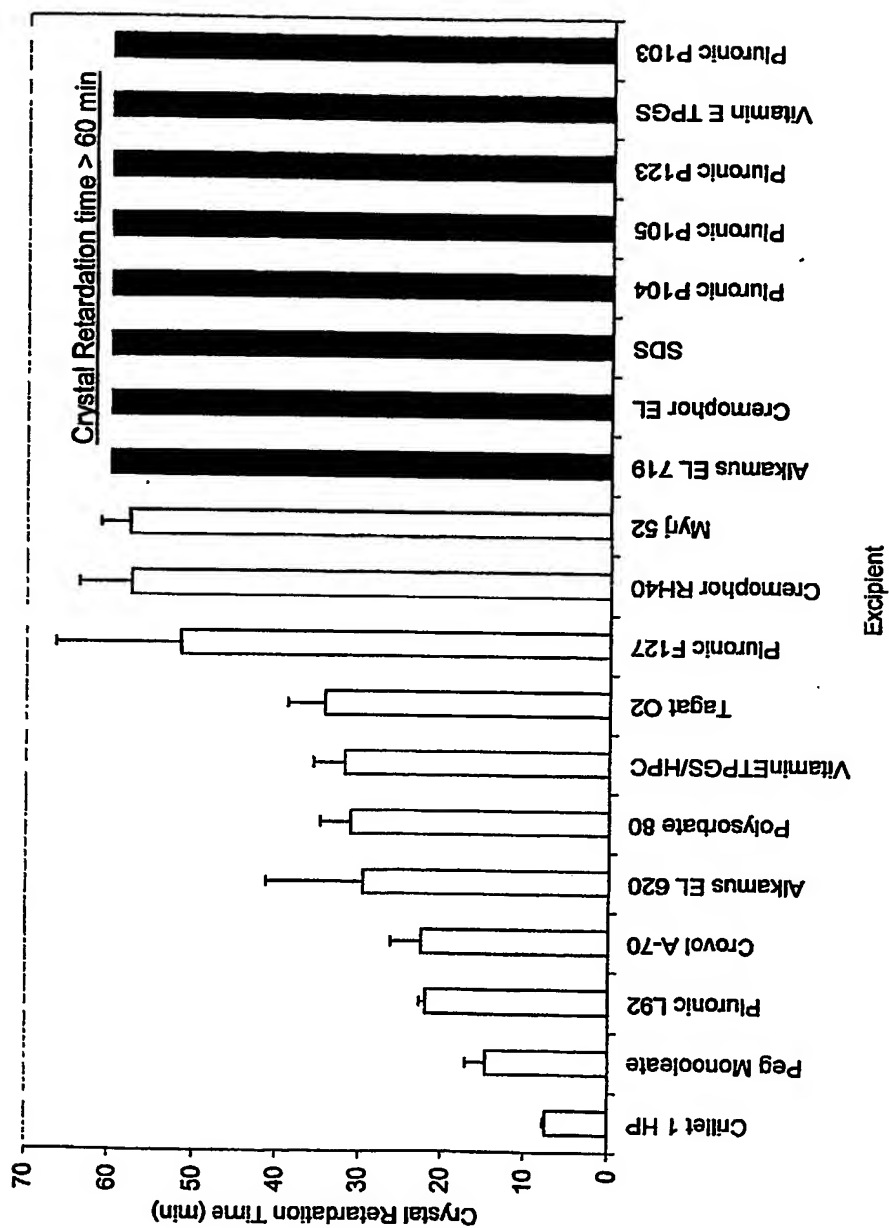


FIG. 30

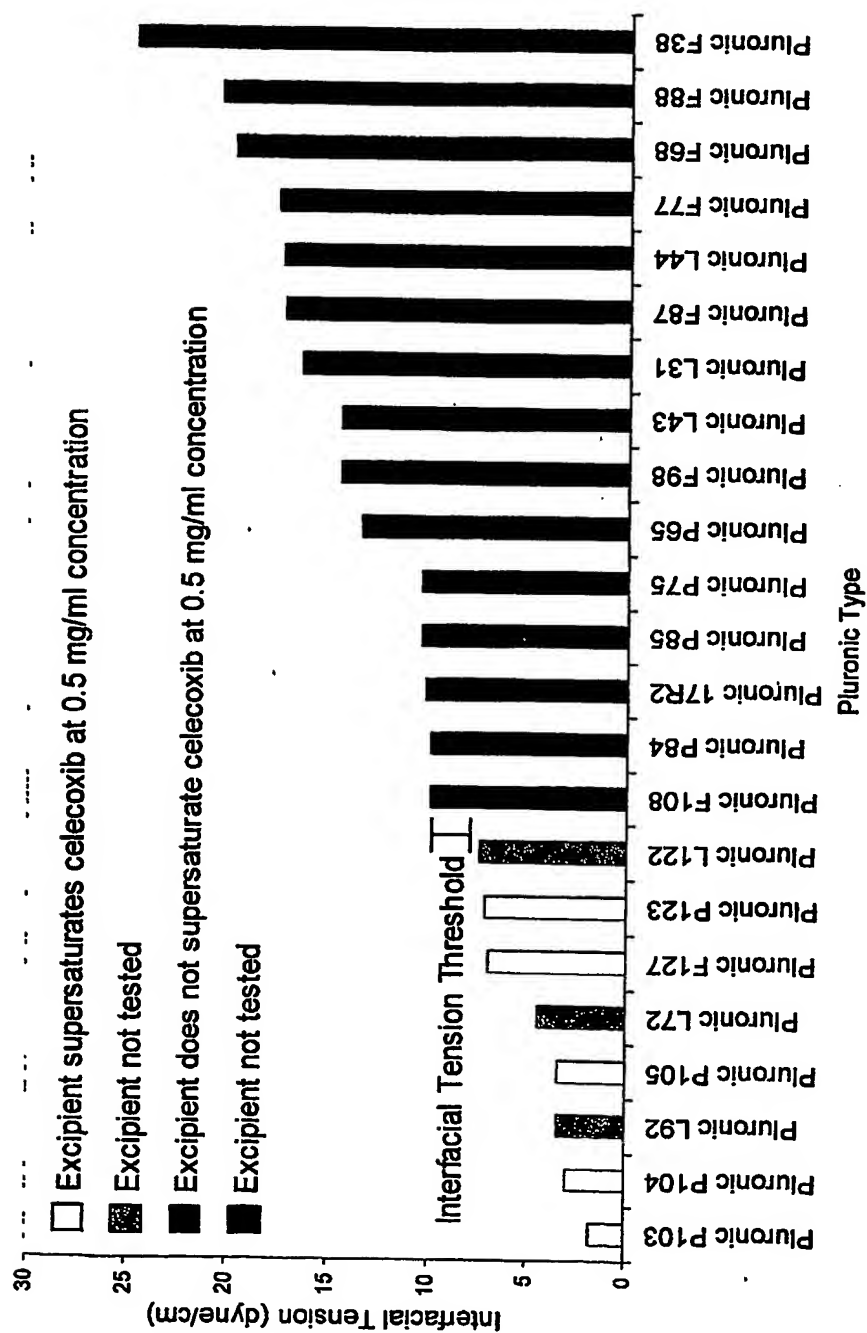


FIG. 31A

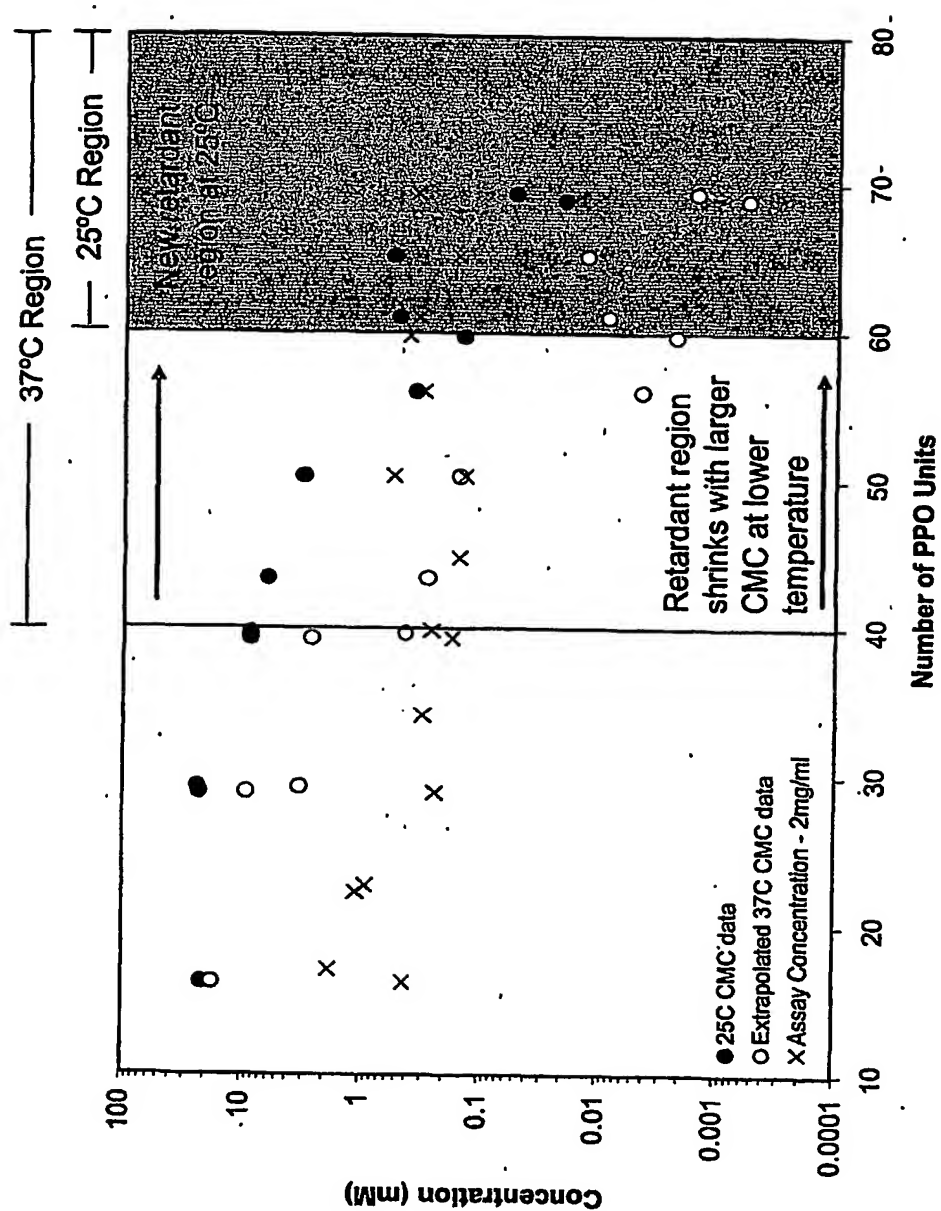


FIG. 31B

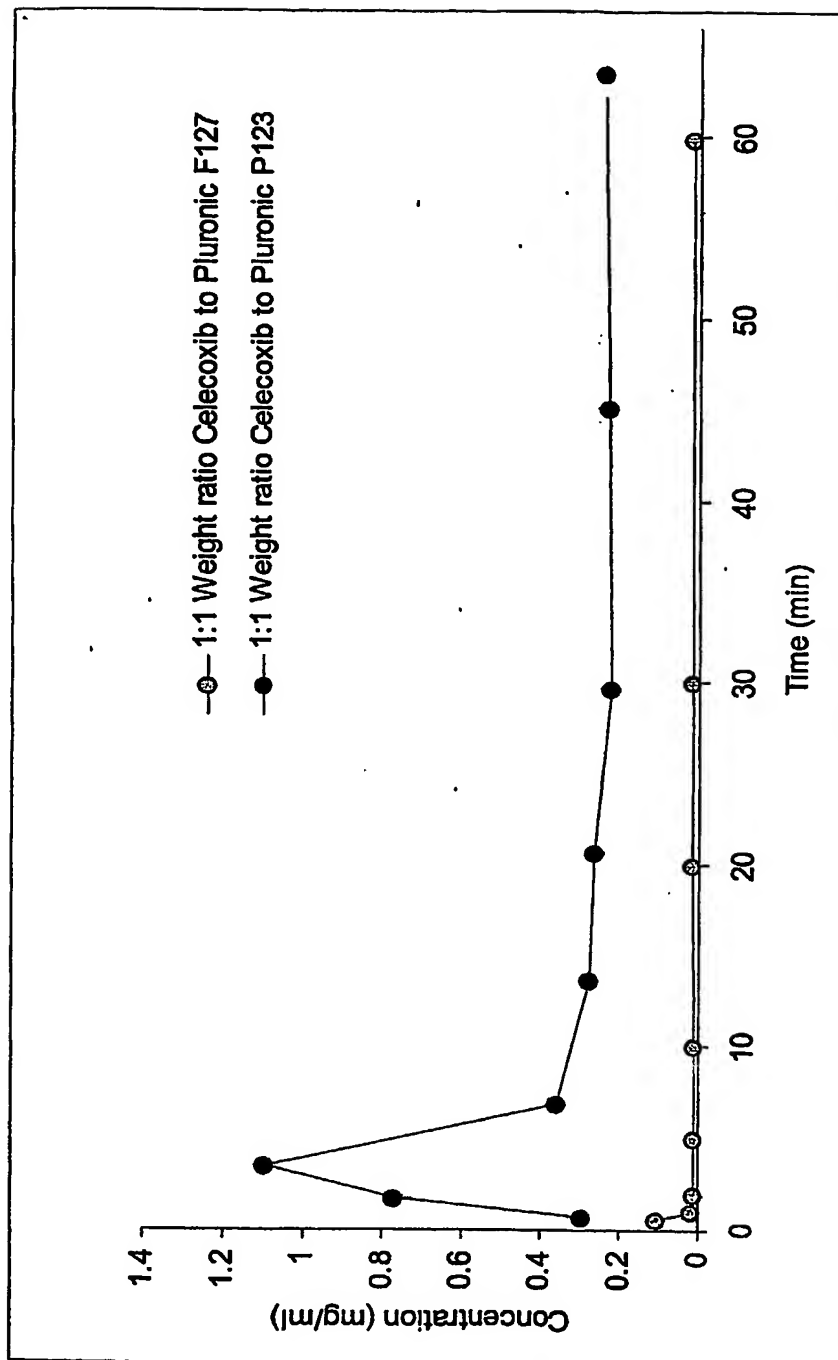


FIG. 32

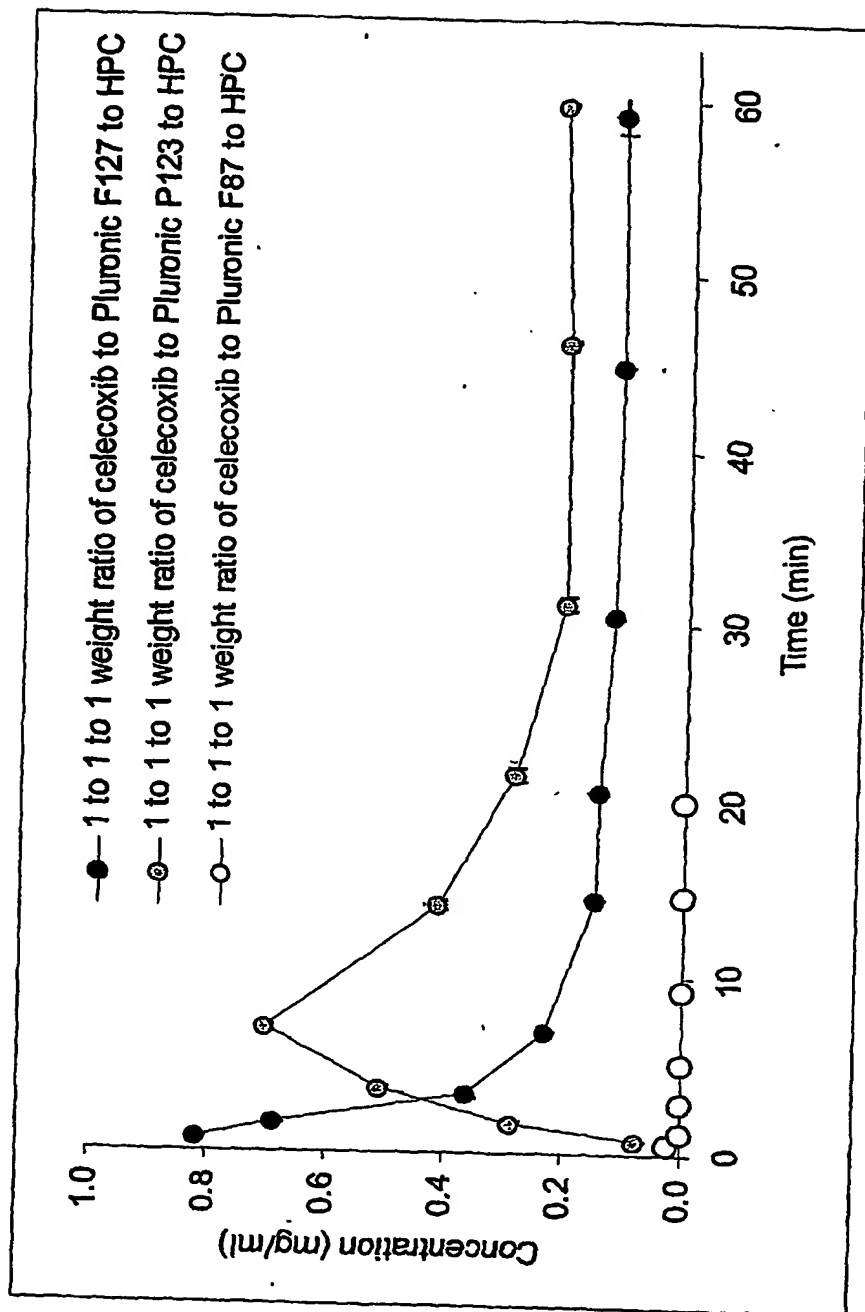


FIG. 33

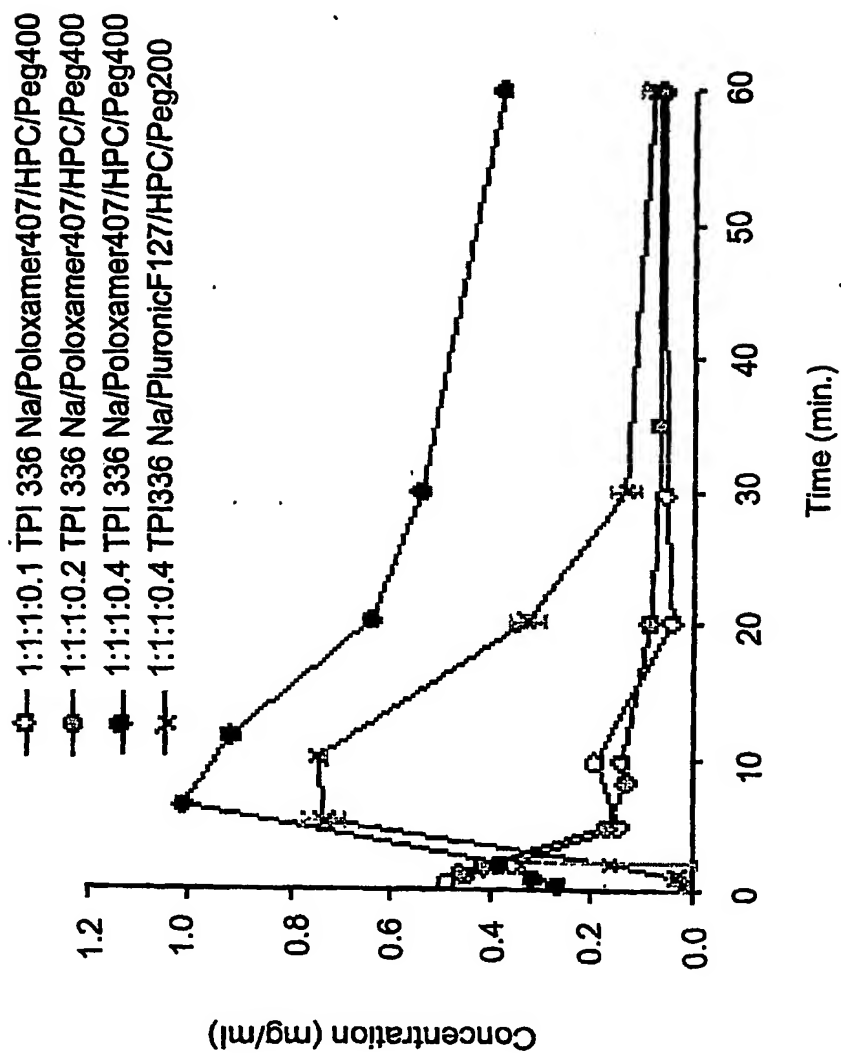


FIG. 34

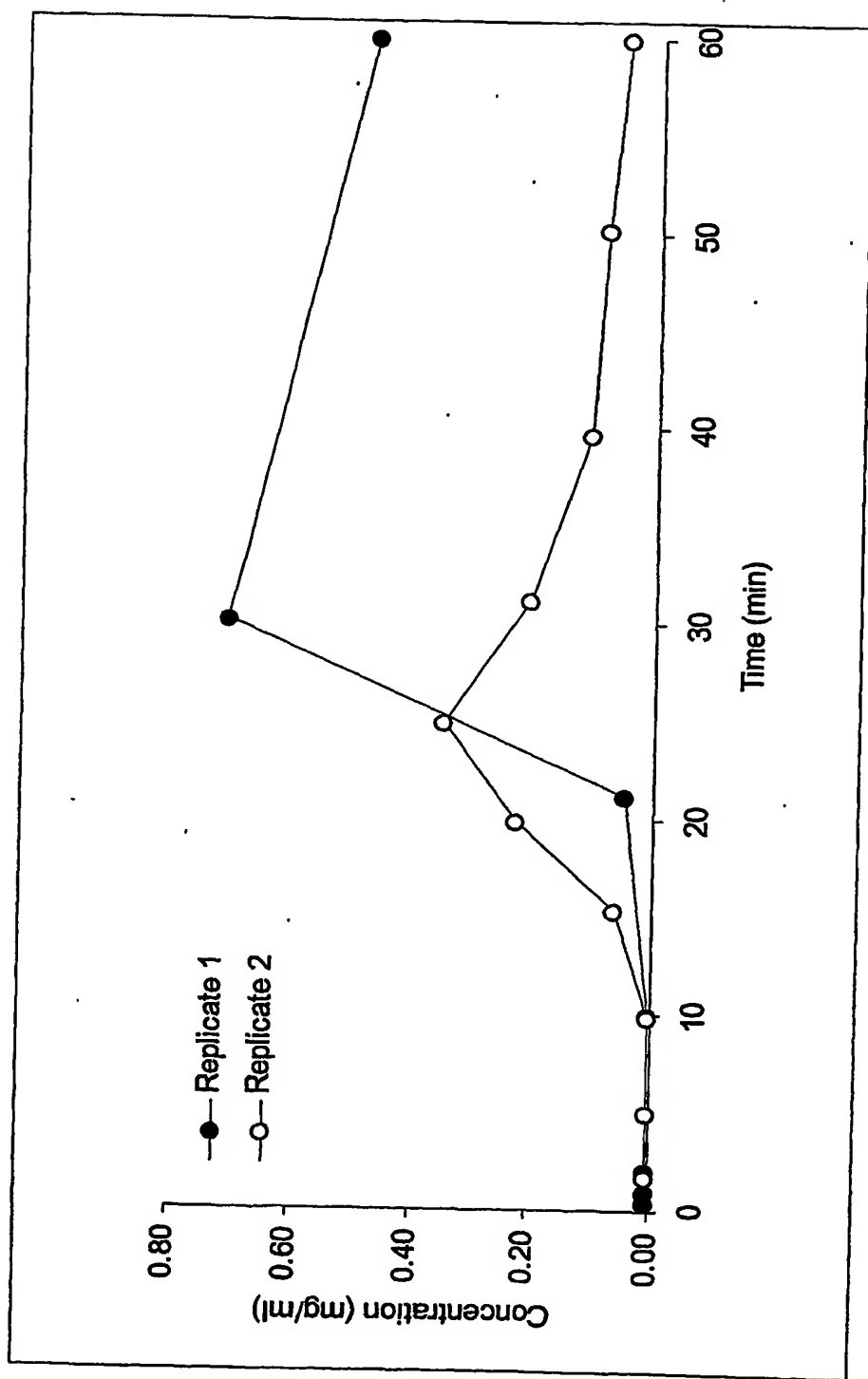


FIG. 35A



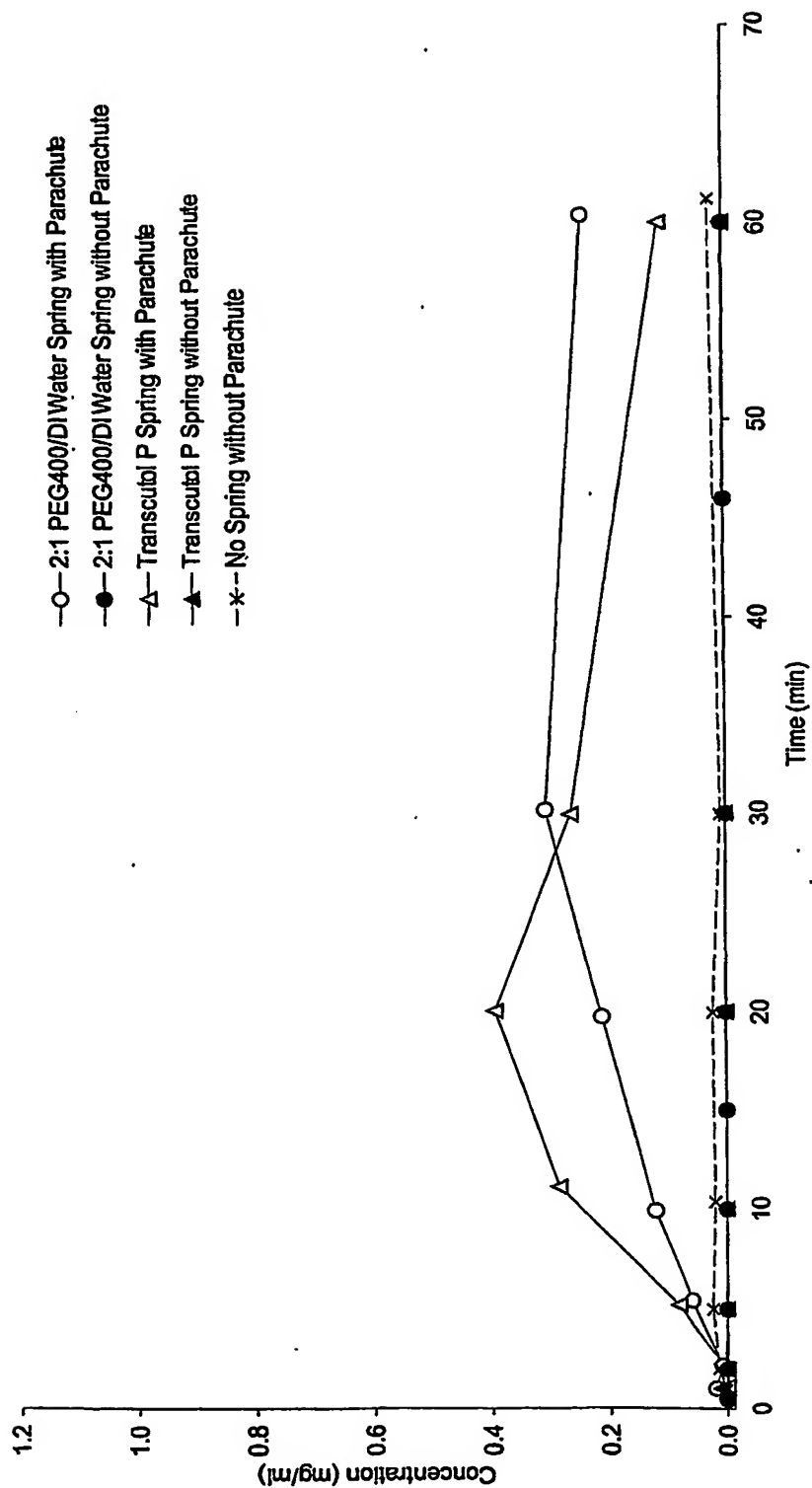


FIG. 35B

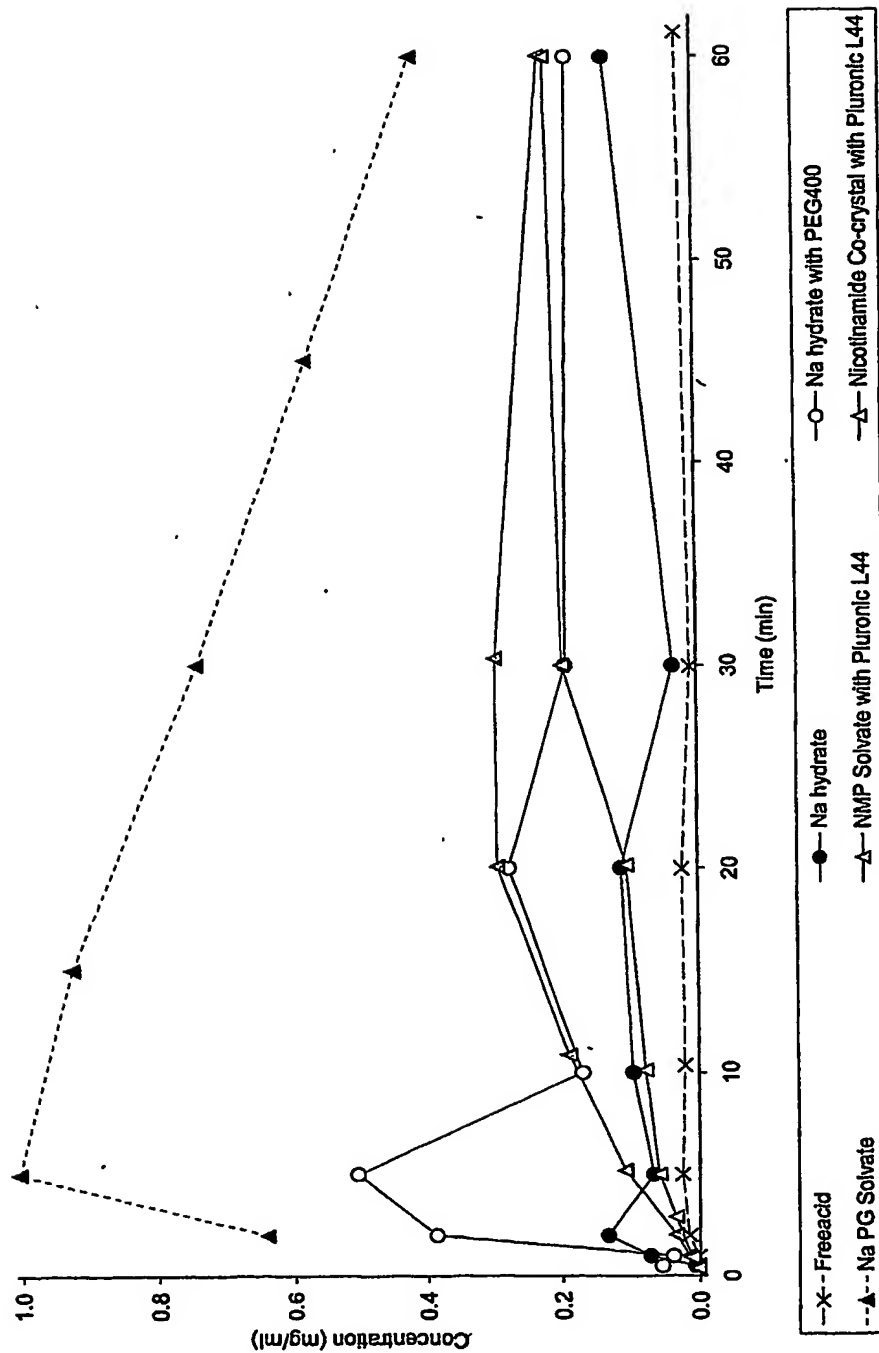


FIG. 35C

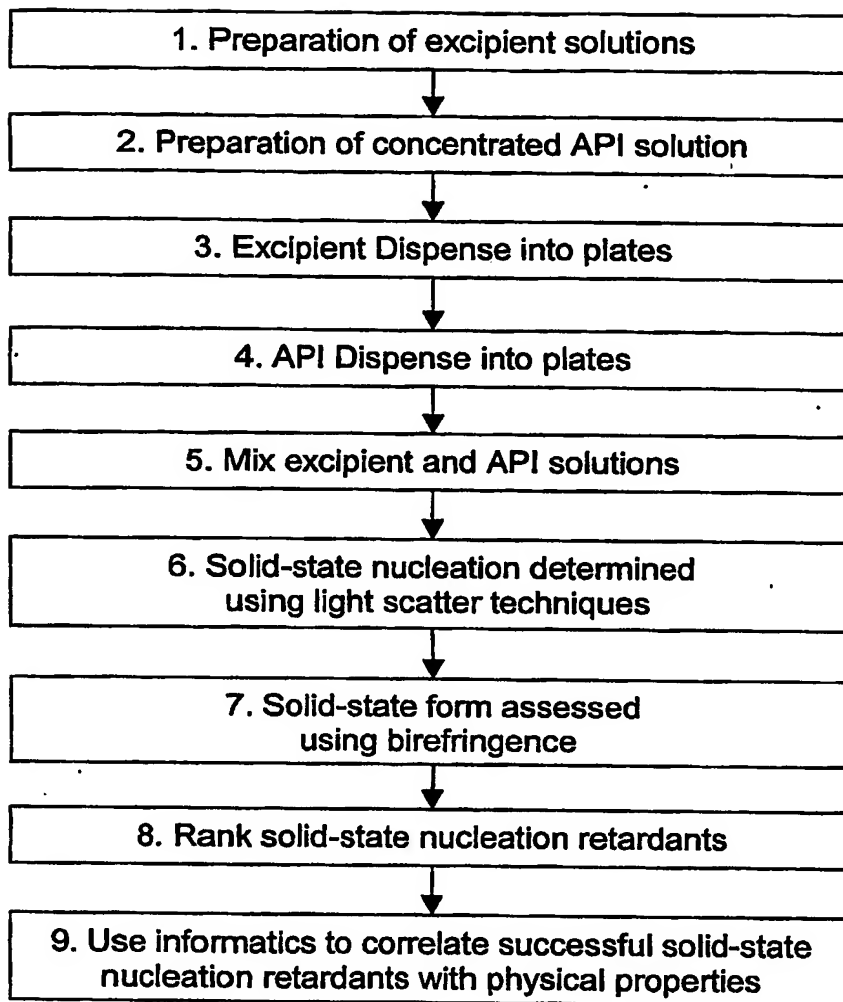


FIG. 36

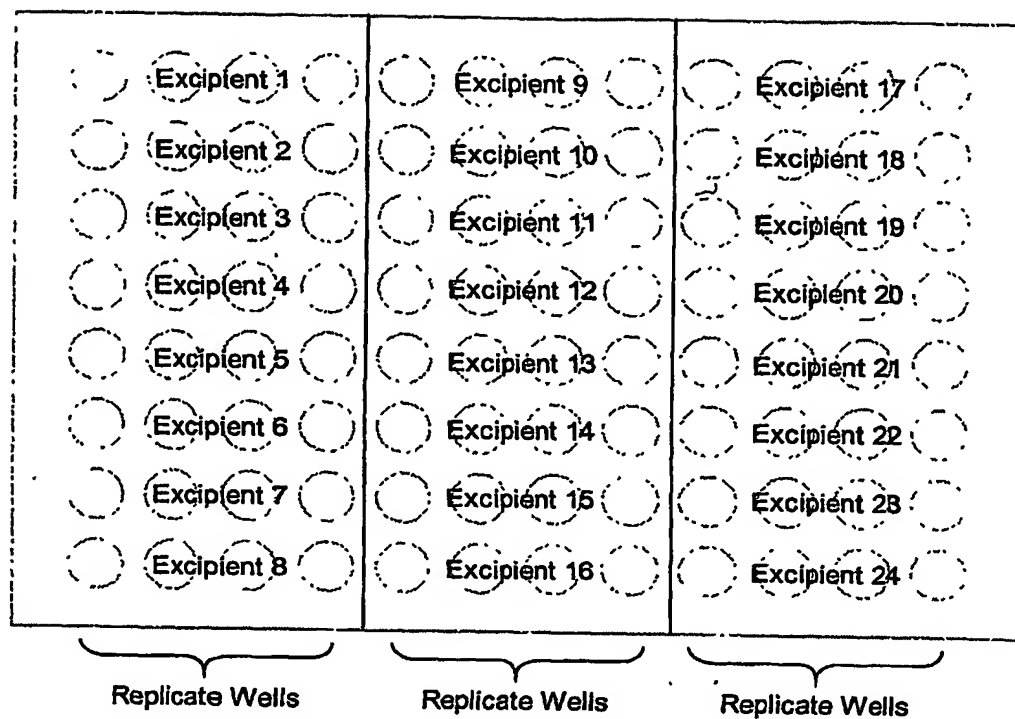


FIG. 37

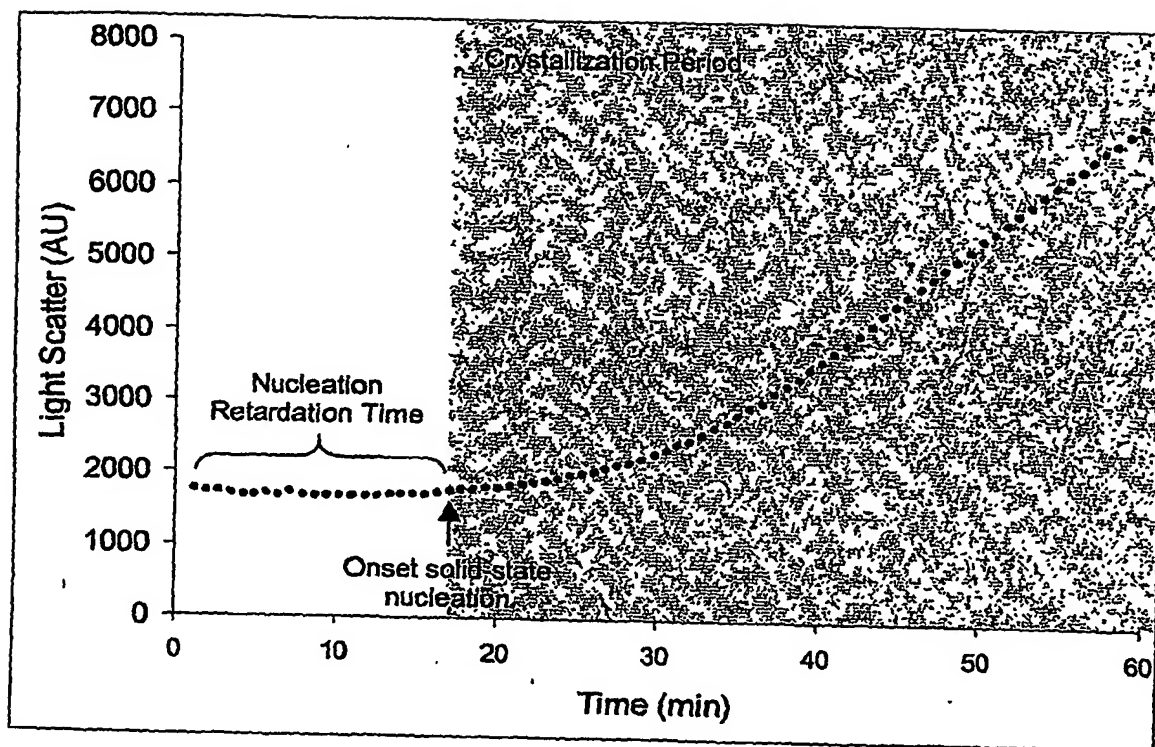


FIG. 38

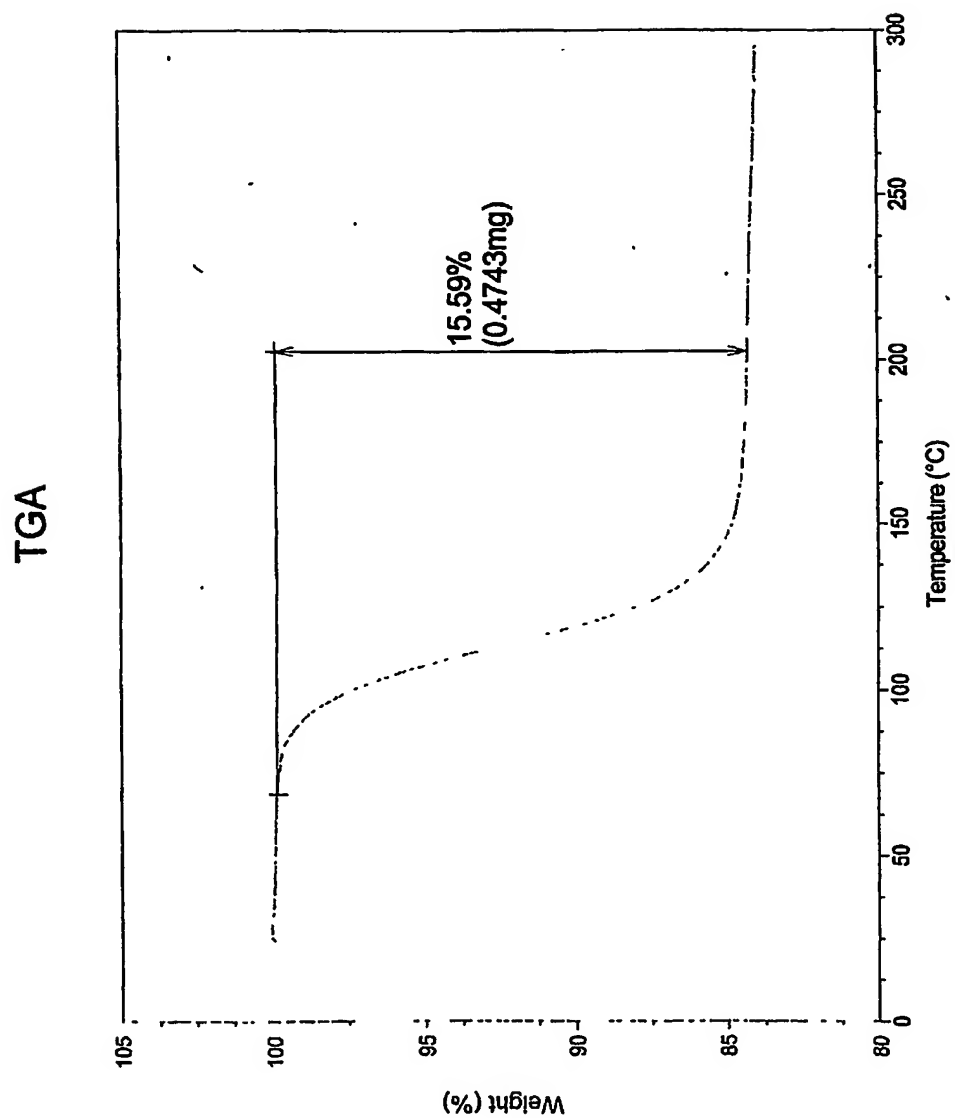


FIG. 39

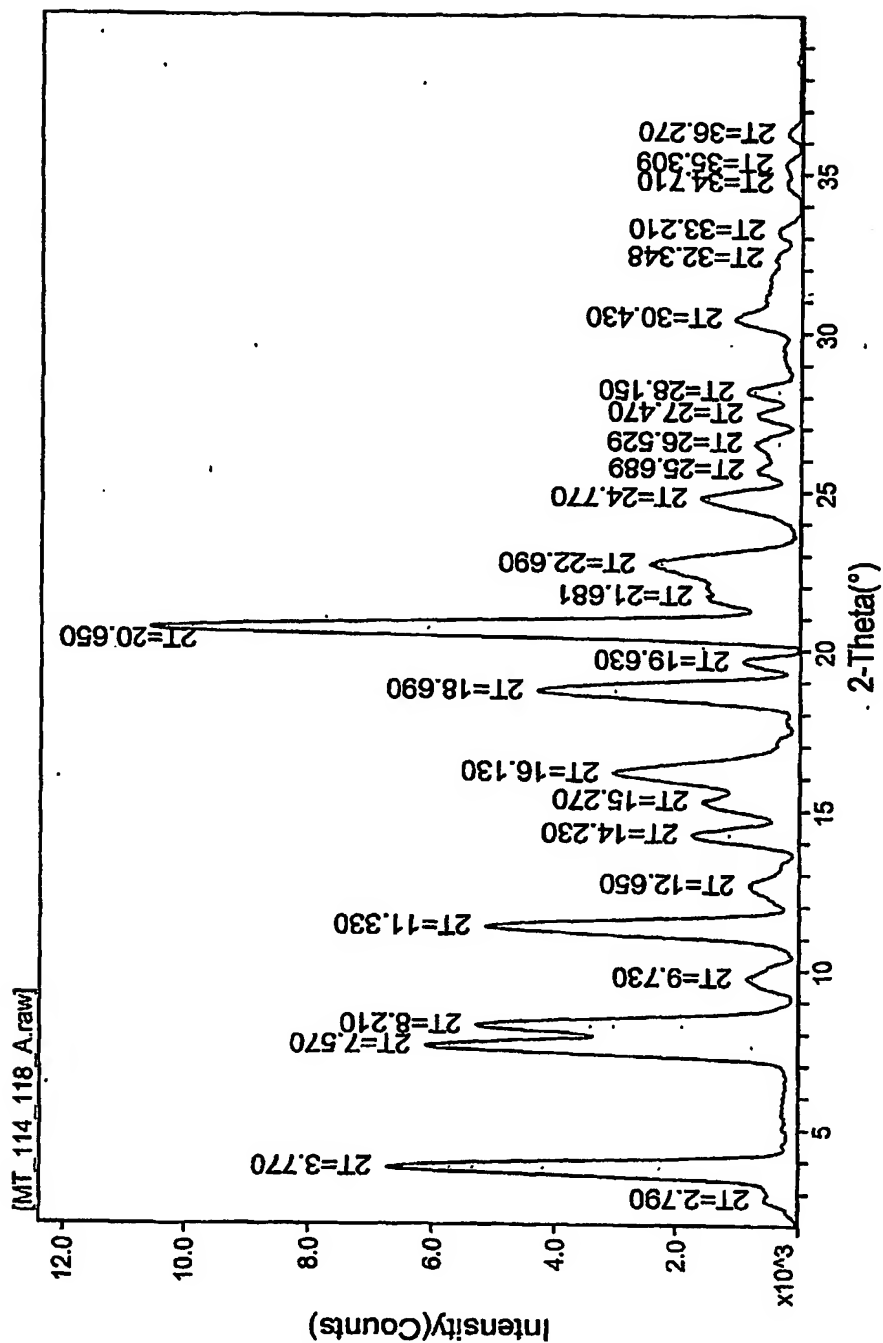


FIG. 40A

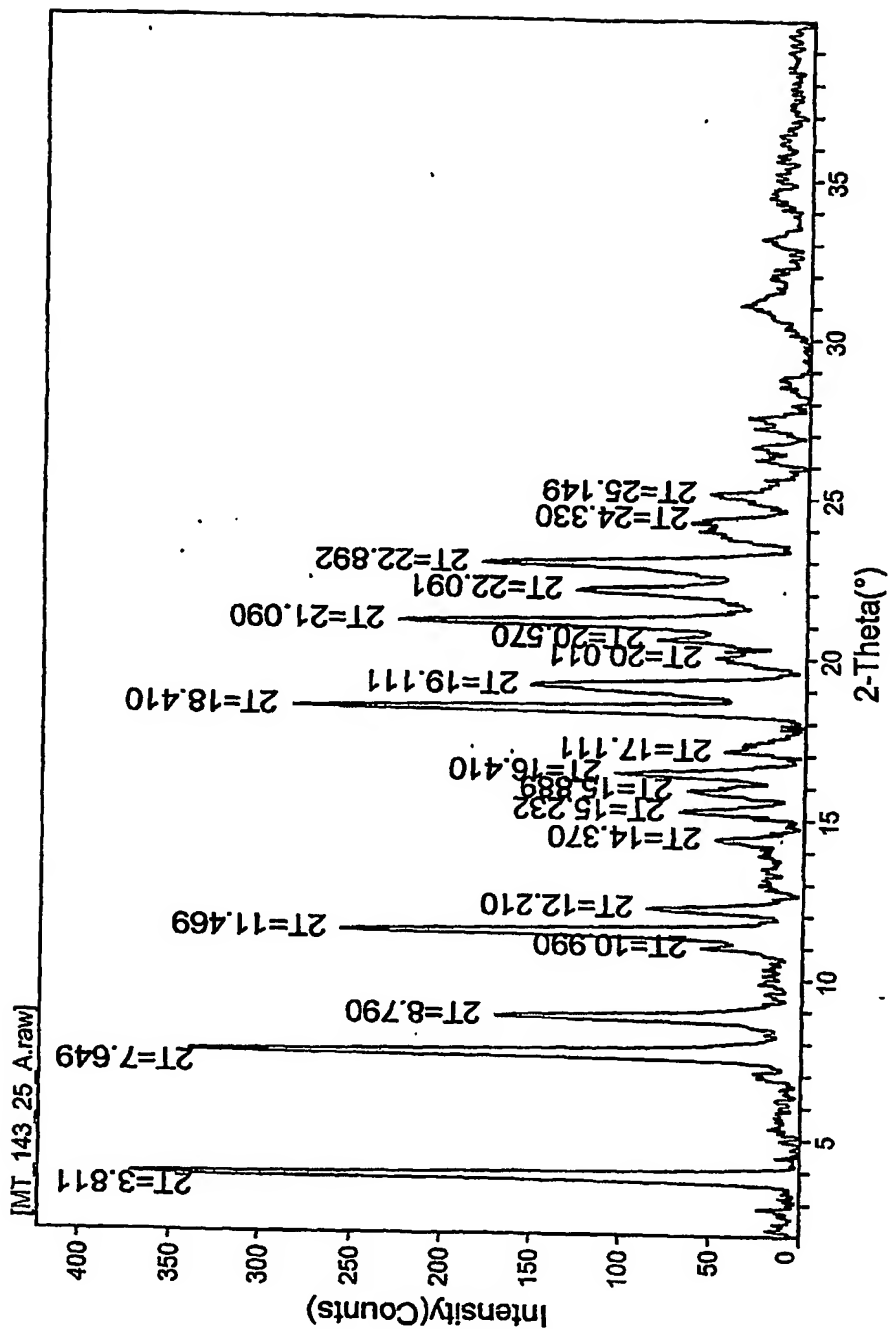


FIG. 40B



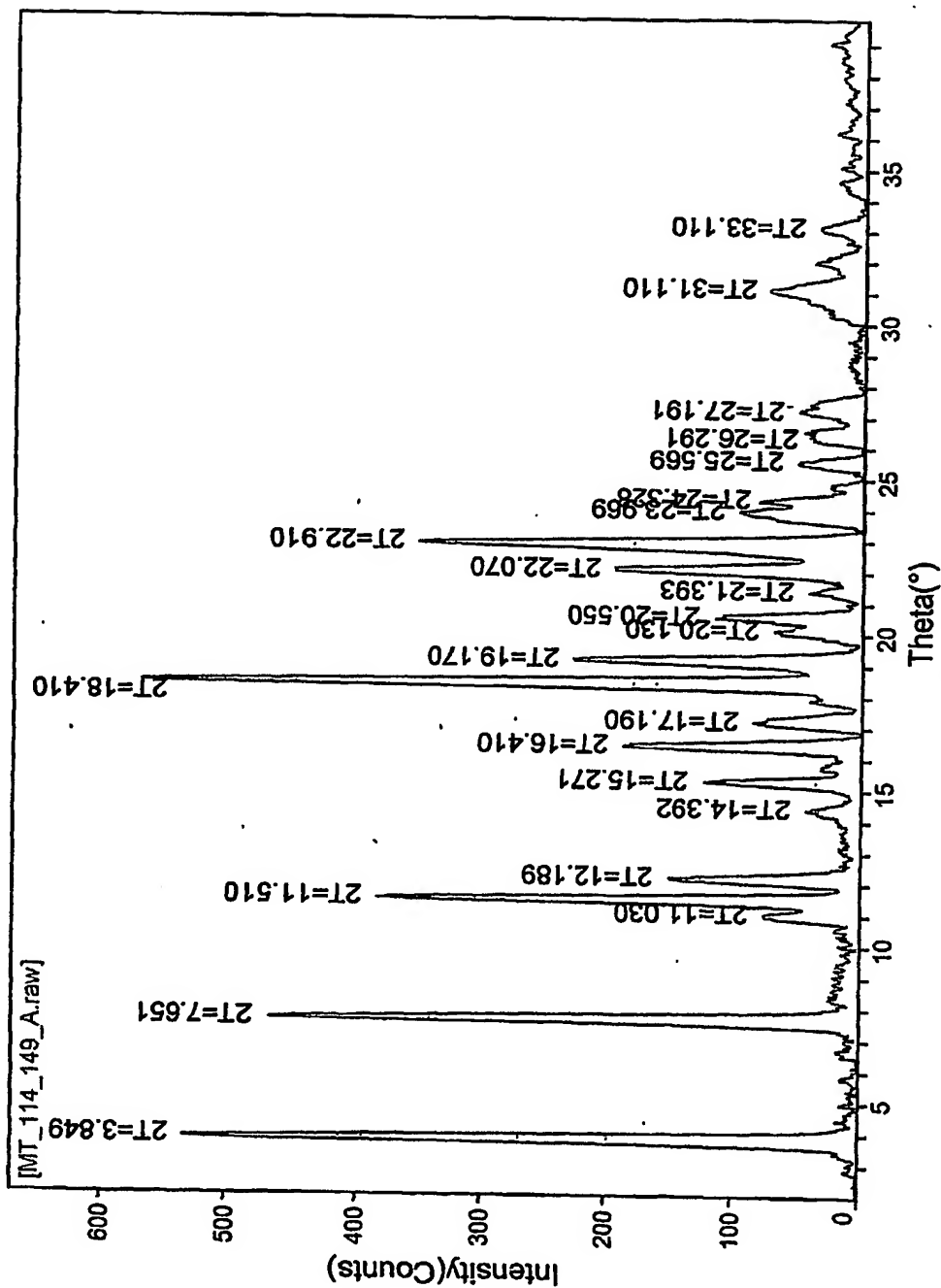


FIG. 40C

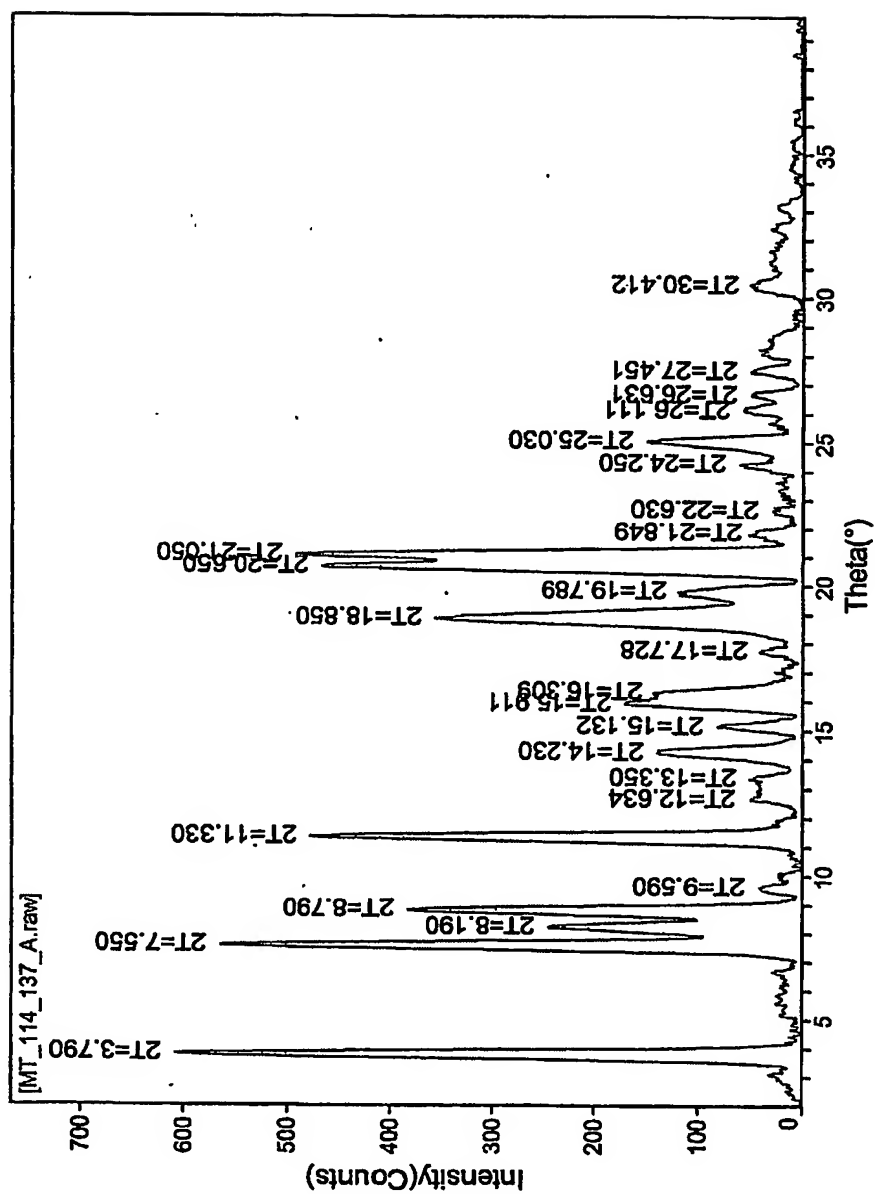


FIG. 40D

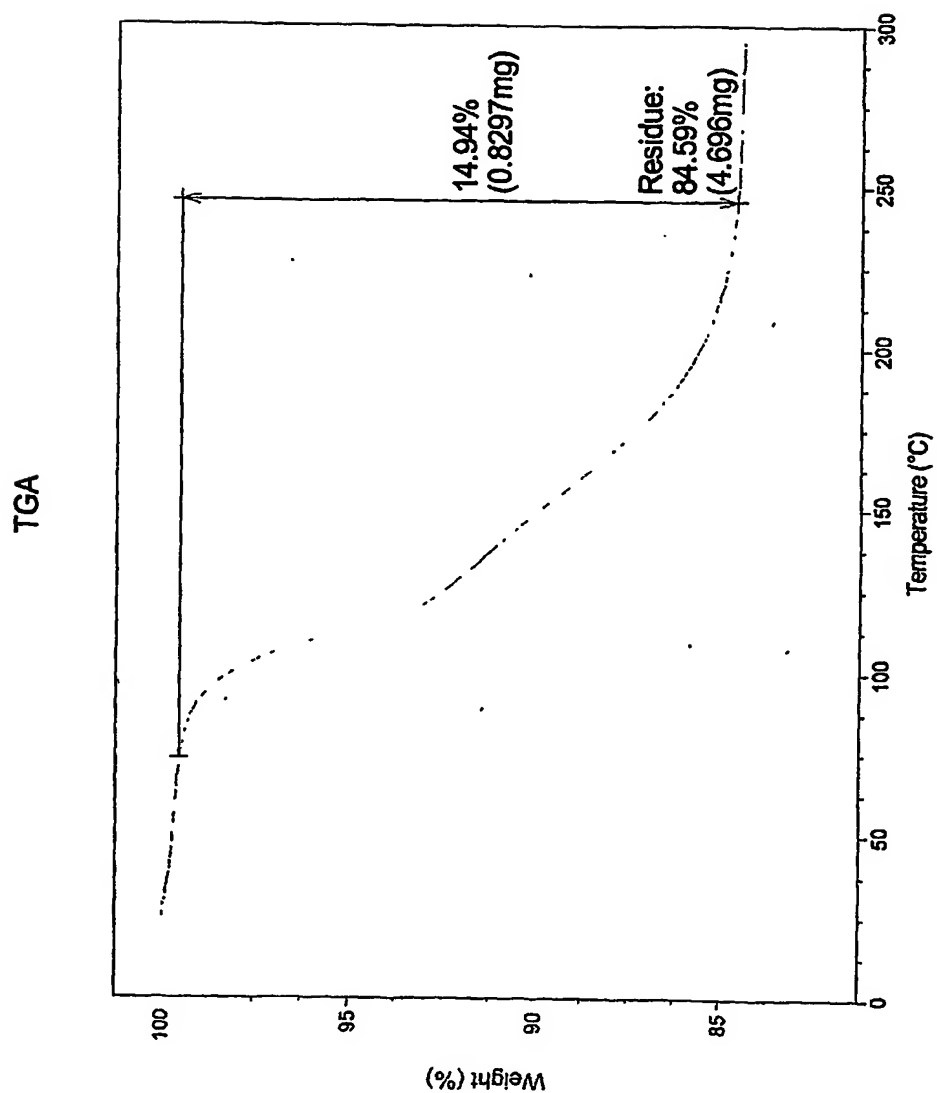


FIG. 41

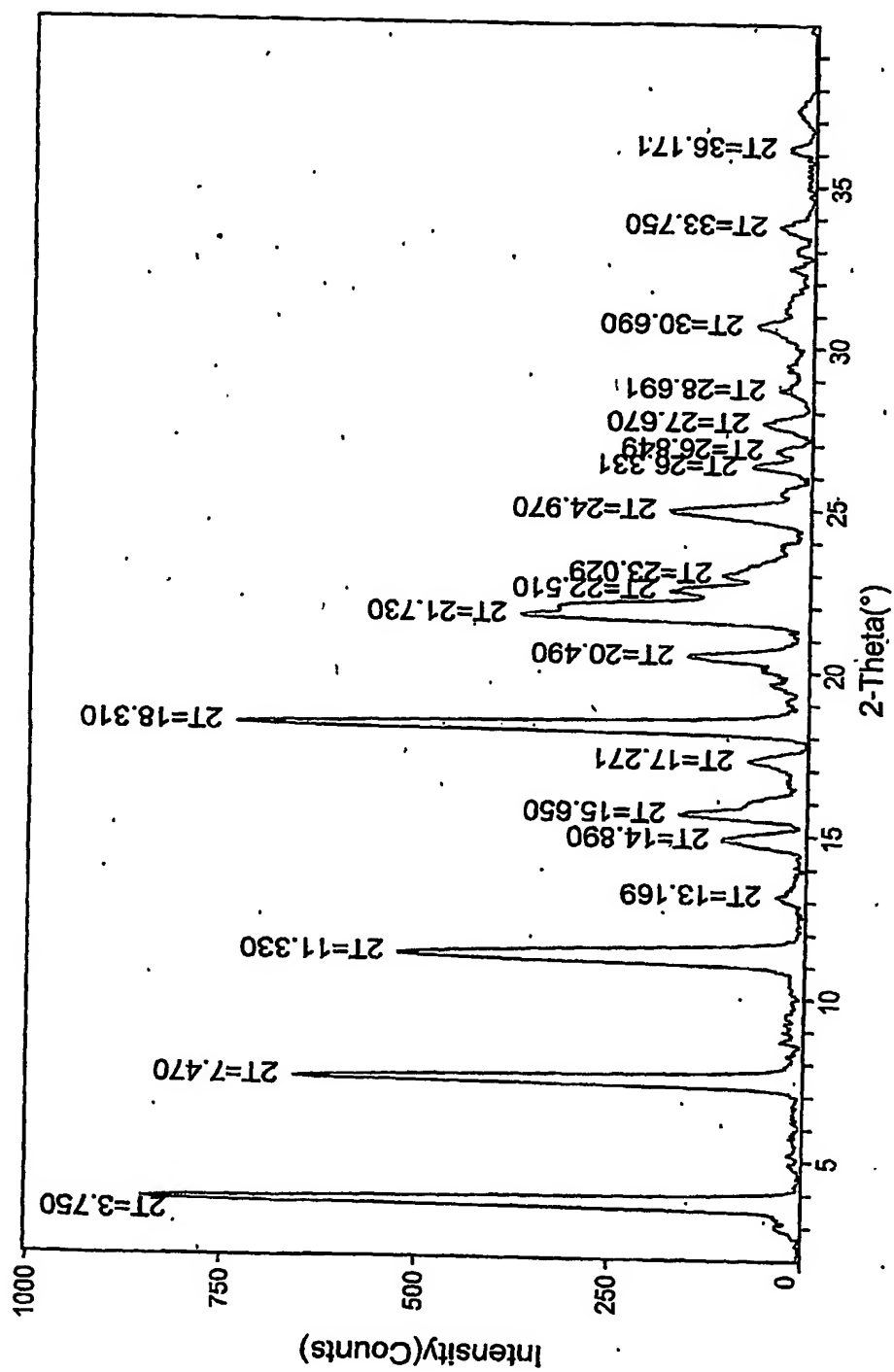


FIG. 42

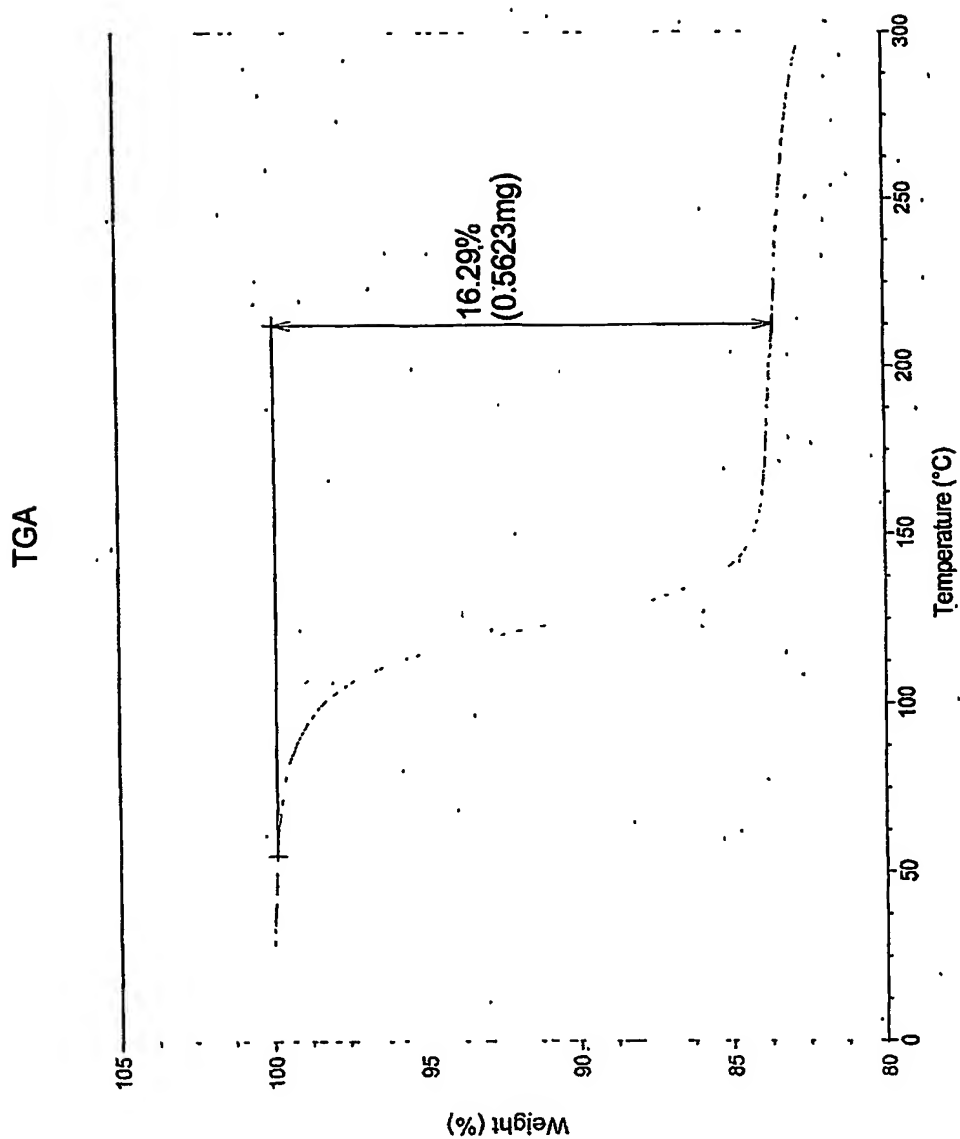


FIG. 43

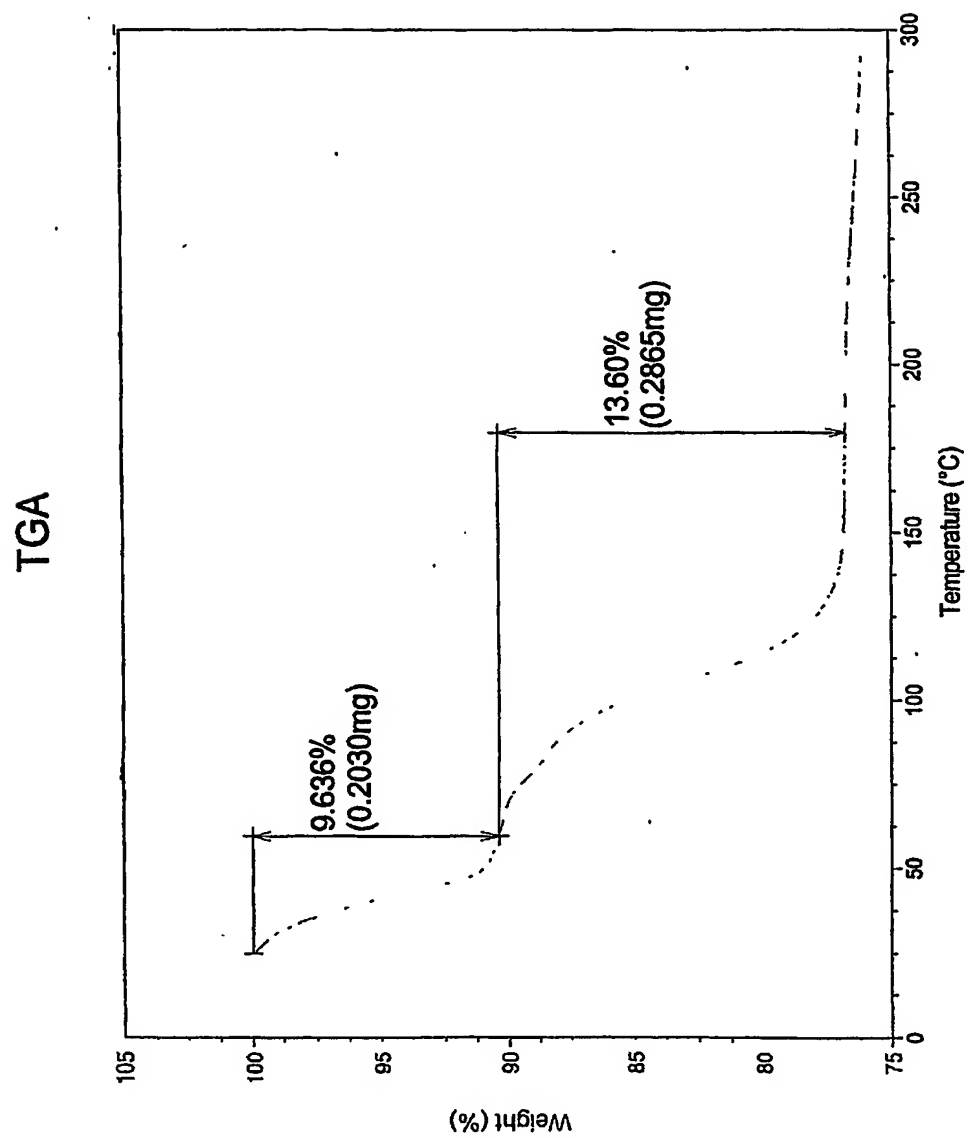


FIG. 44

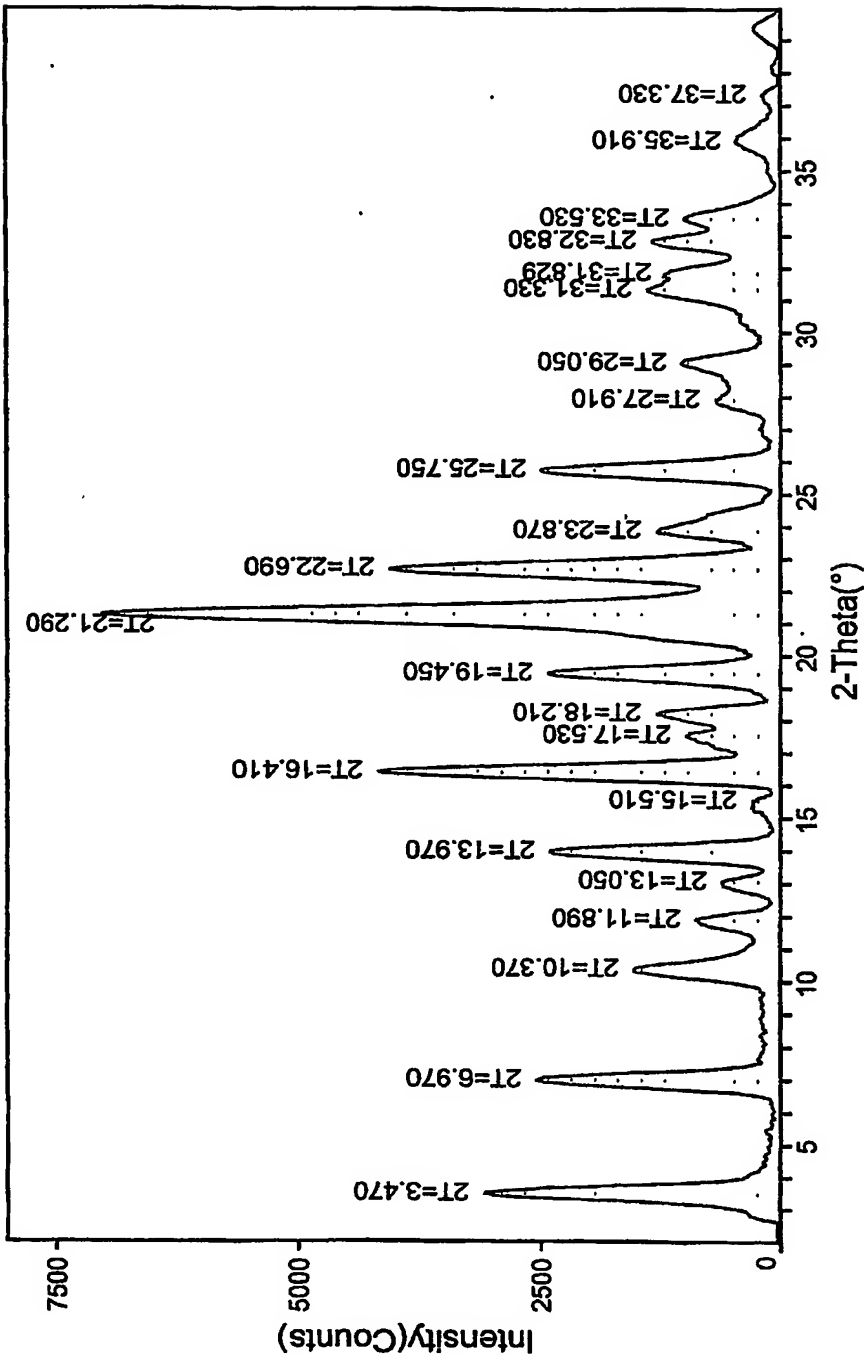


FIG. 45

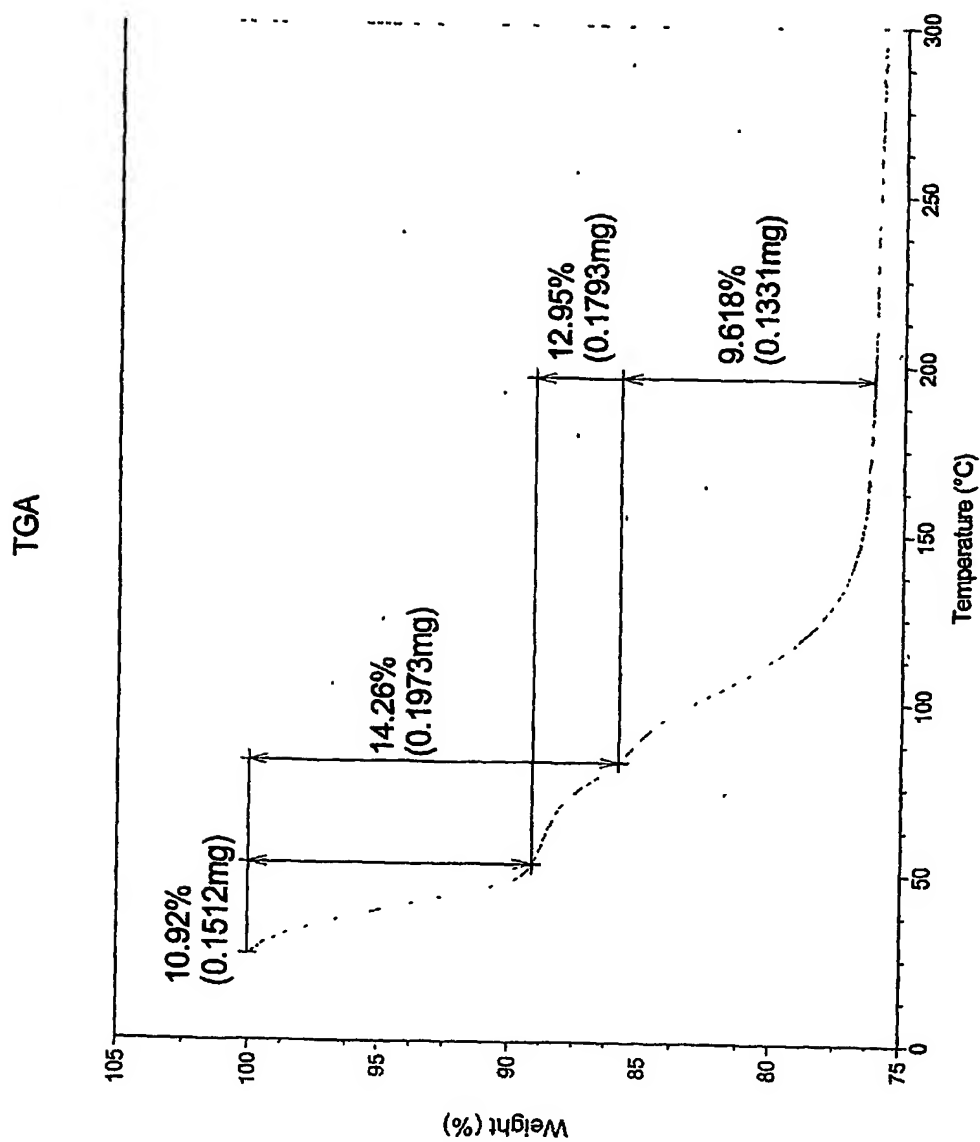


FIG. 46



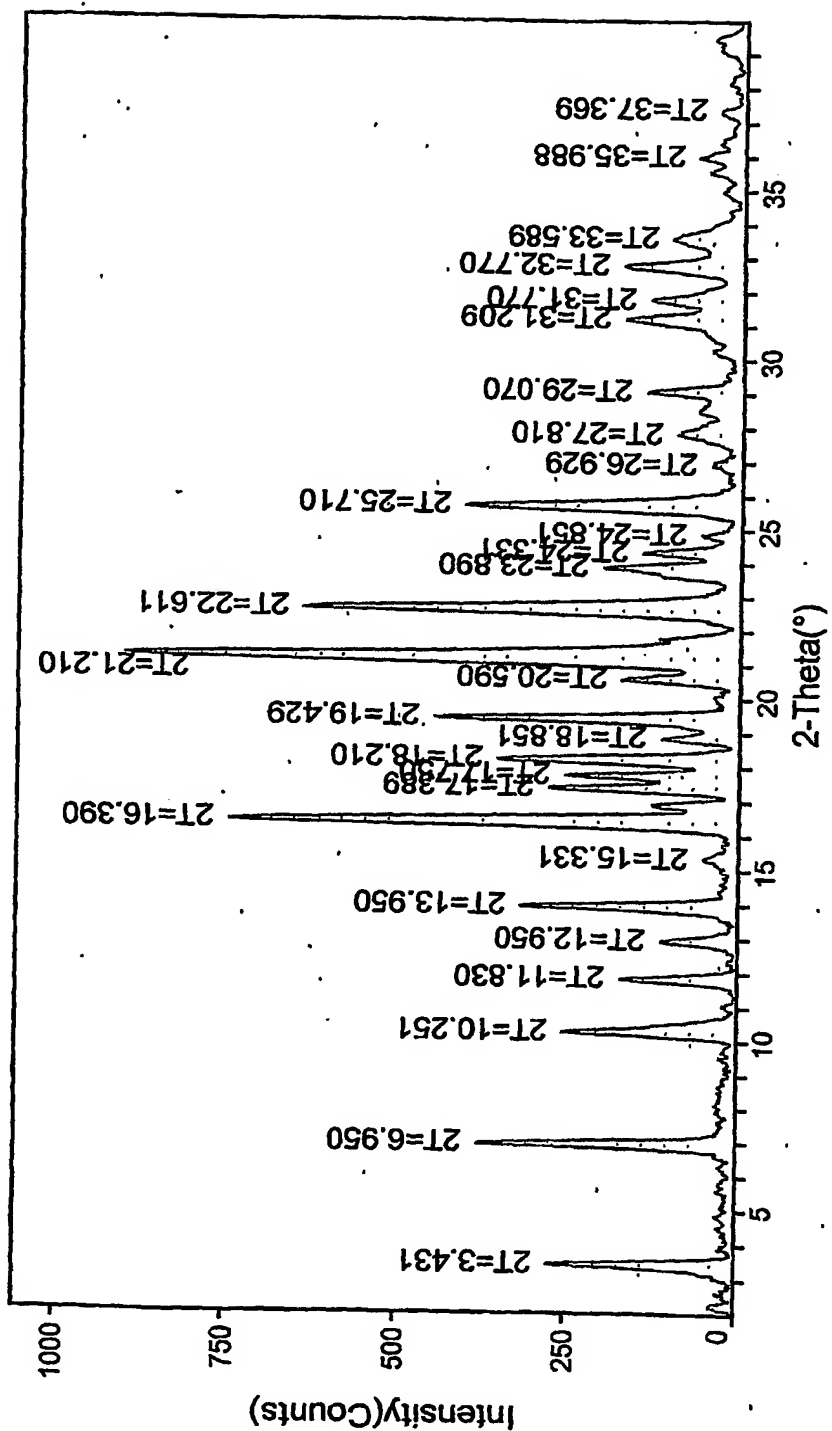


FIG. 47

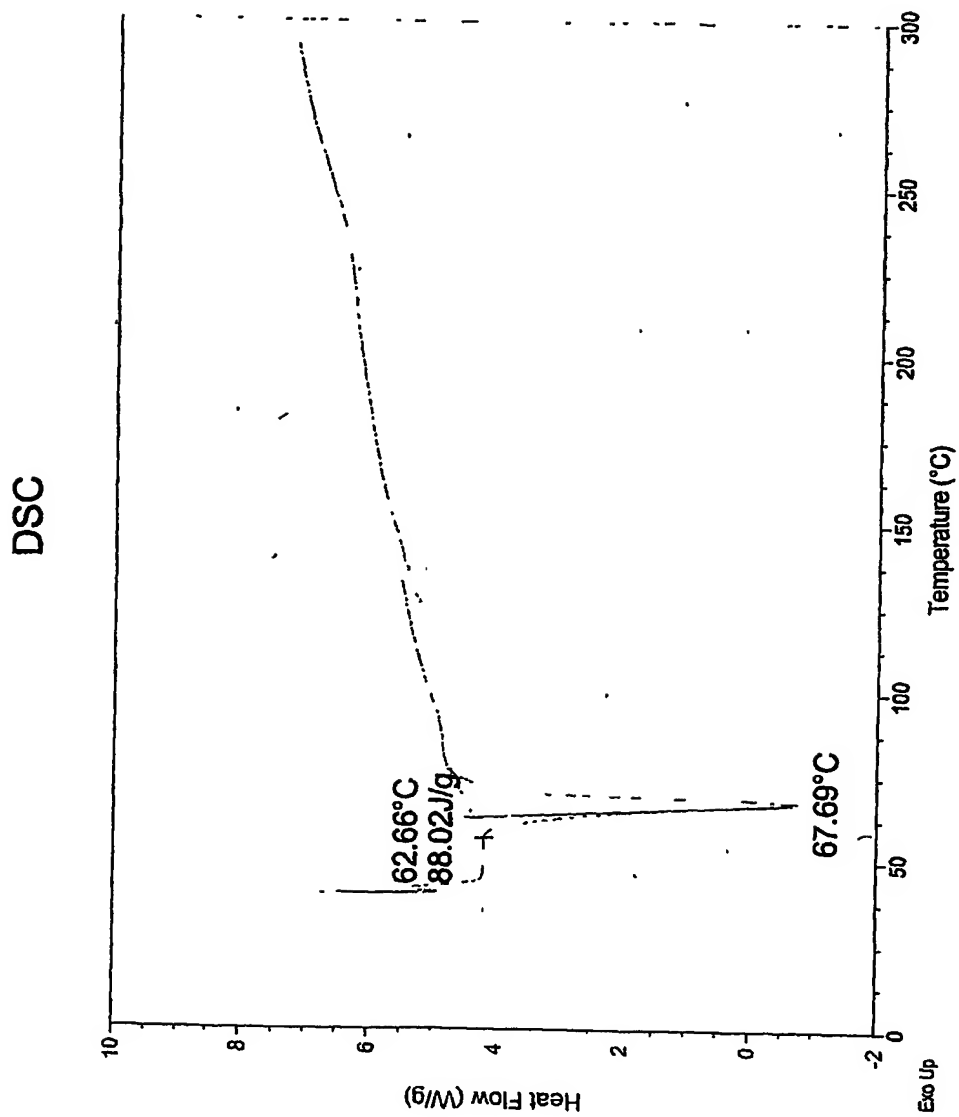


FIG. 48

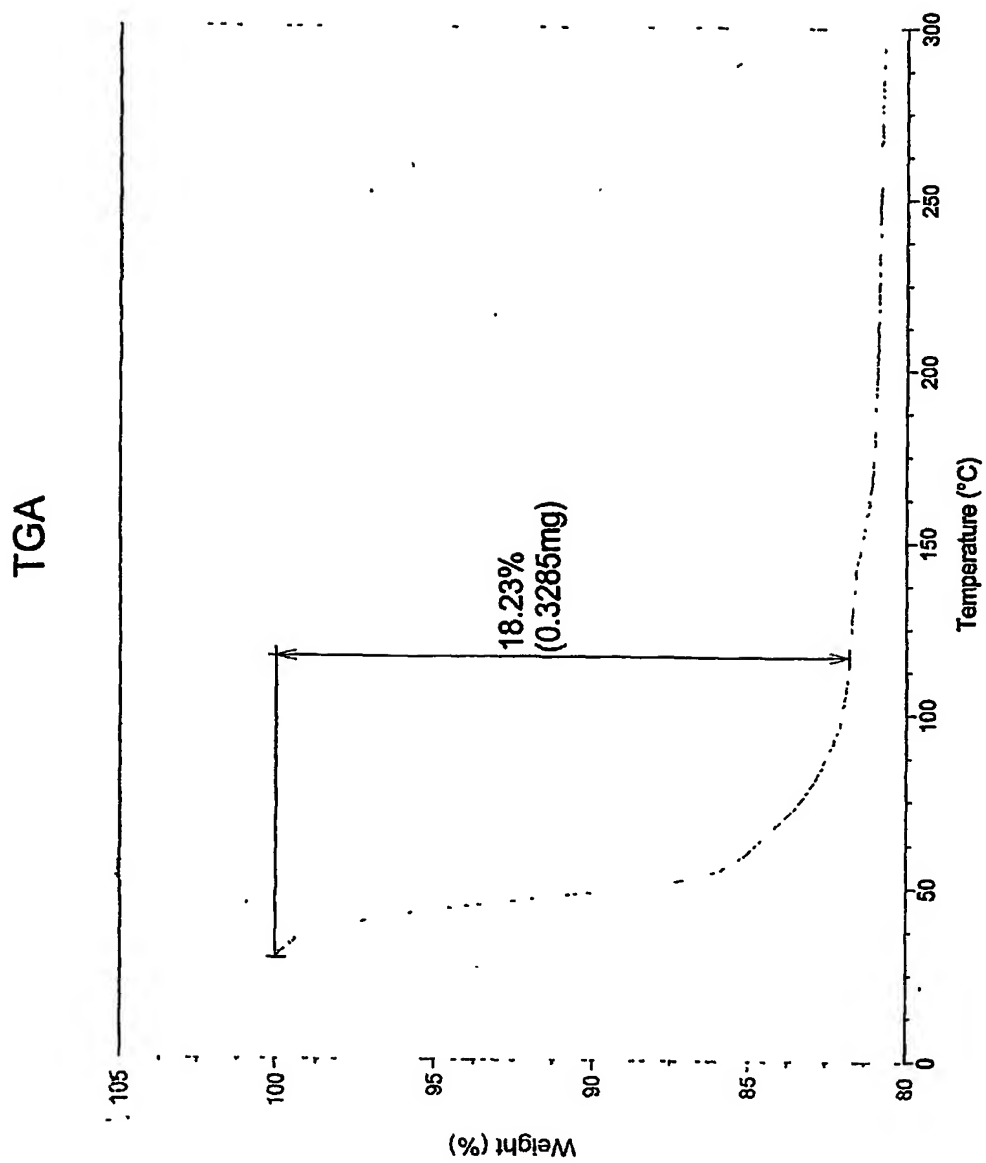


FIG. 49

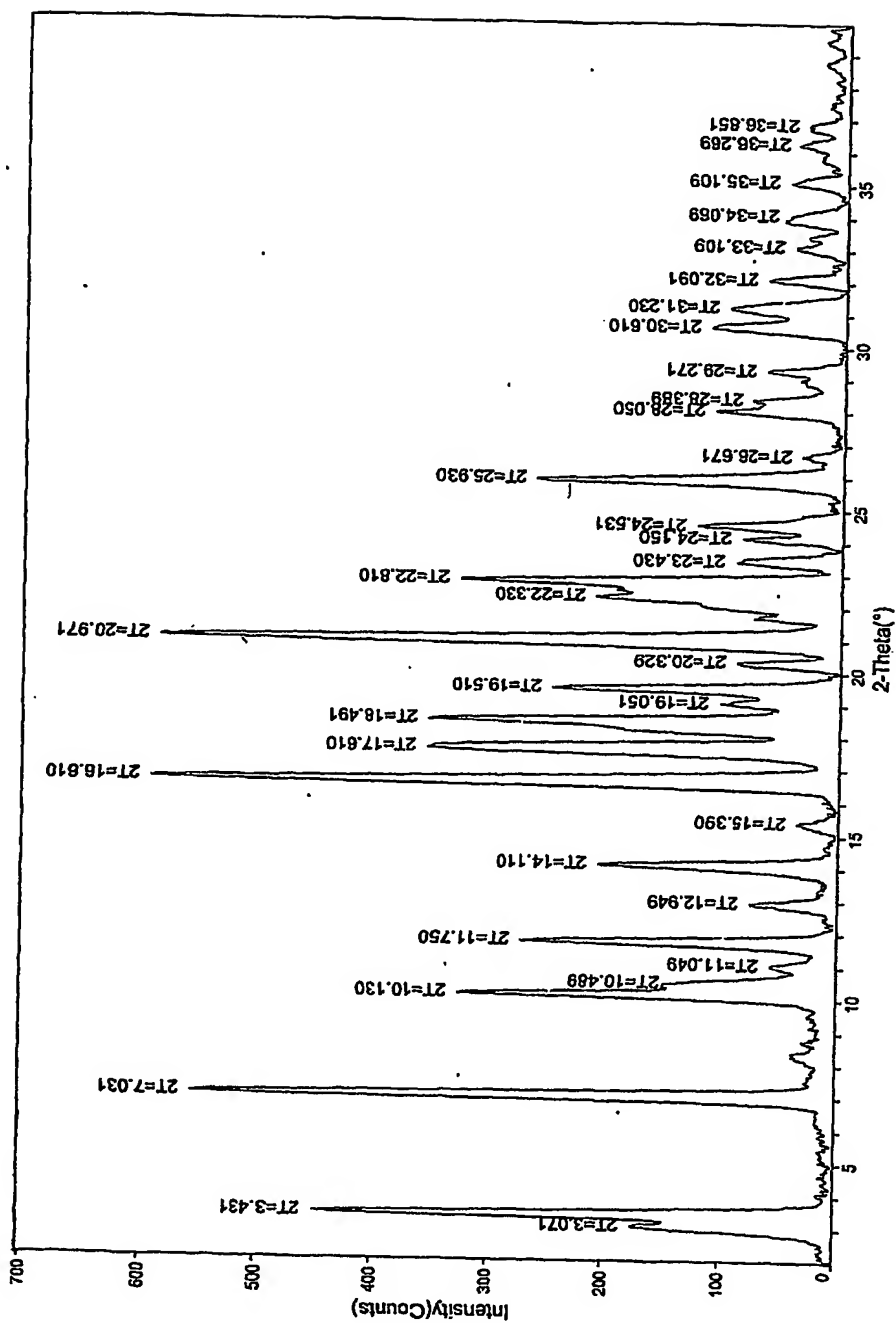


FIG. 50

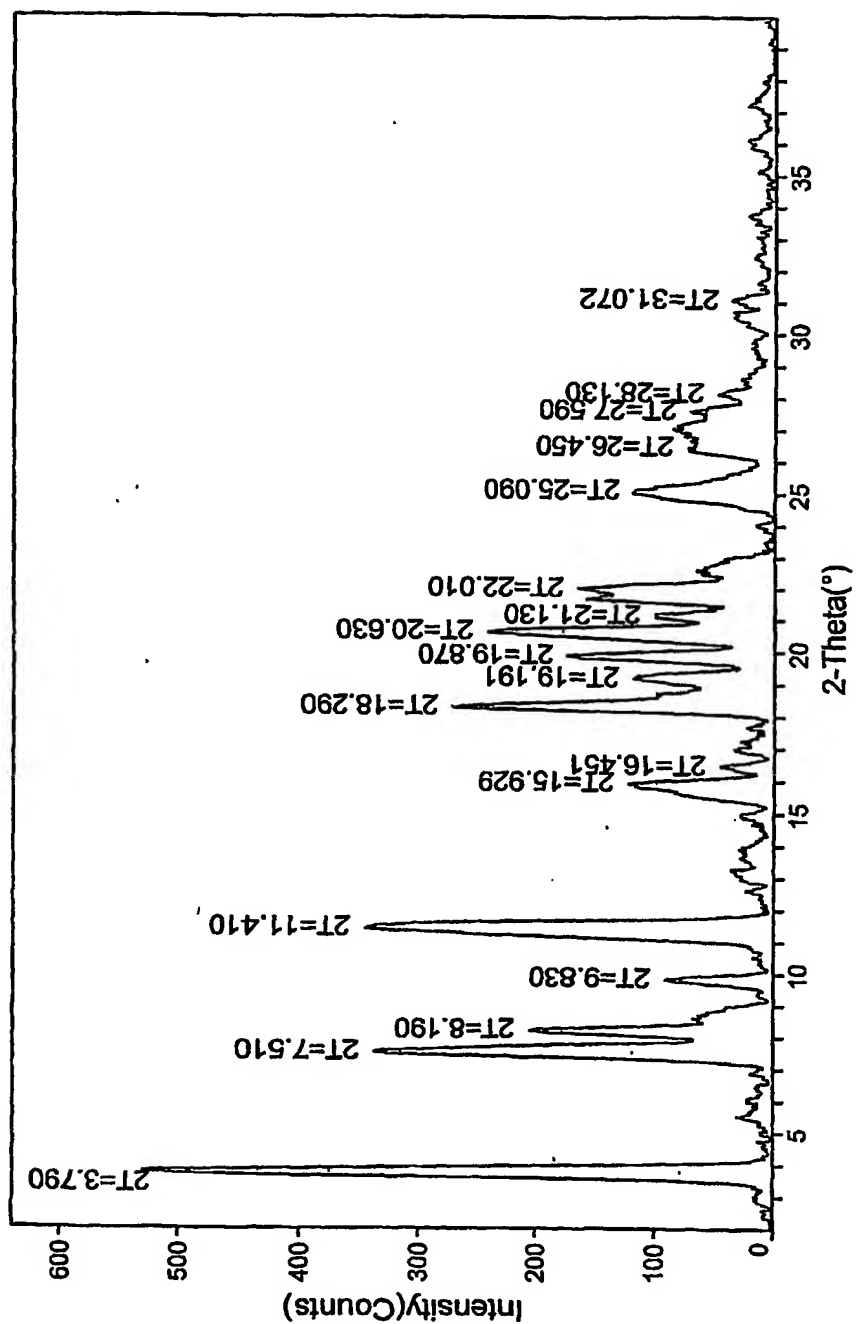


FIG. 51

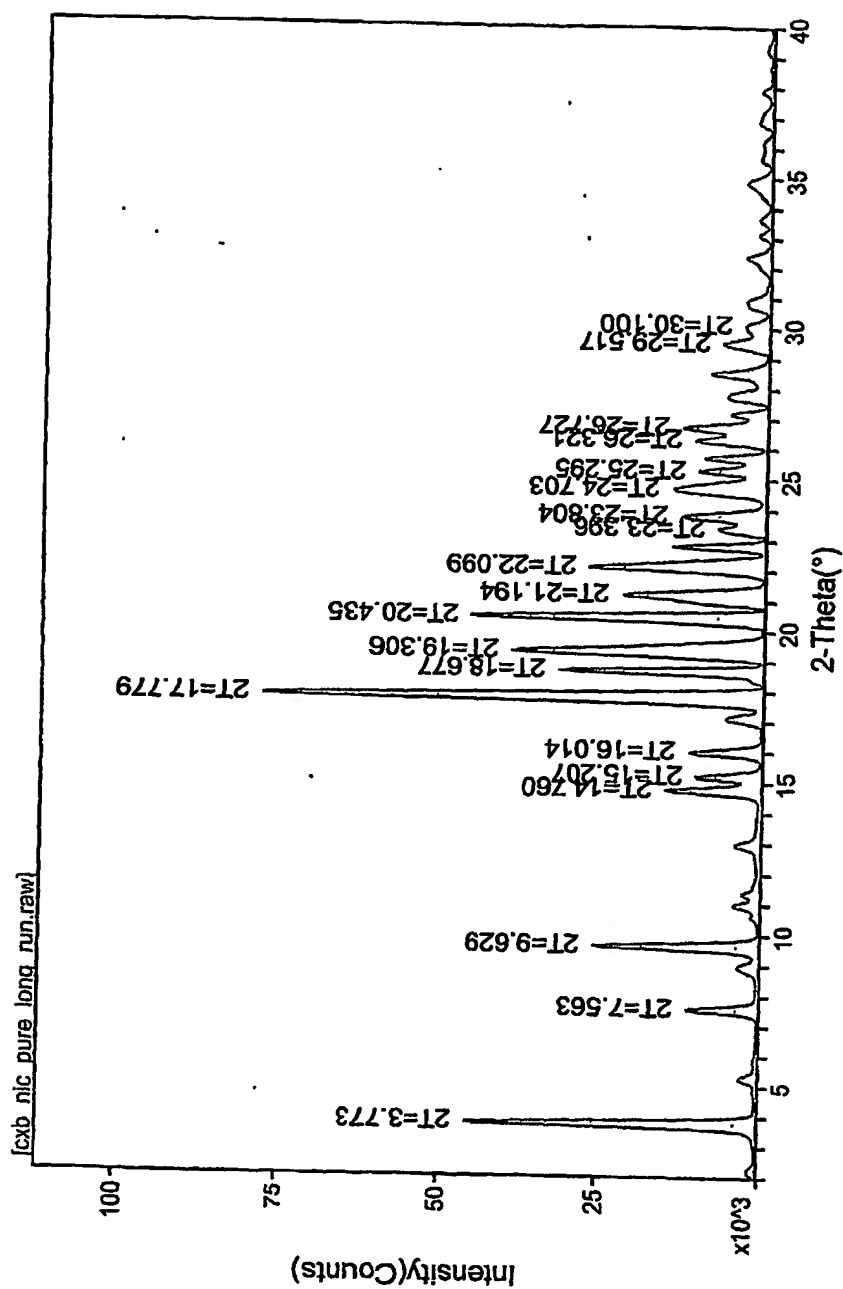


FIG. 52

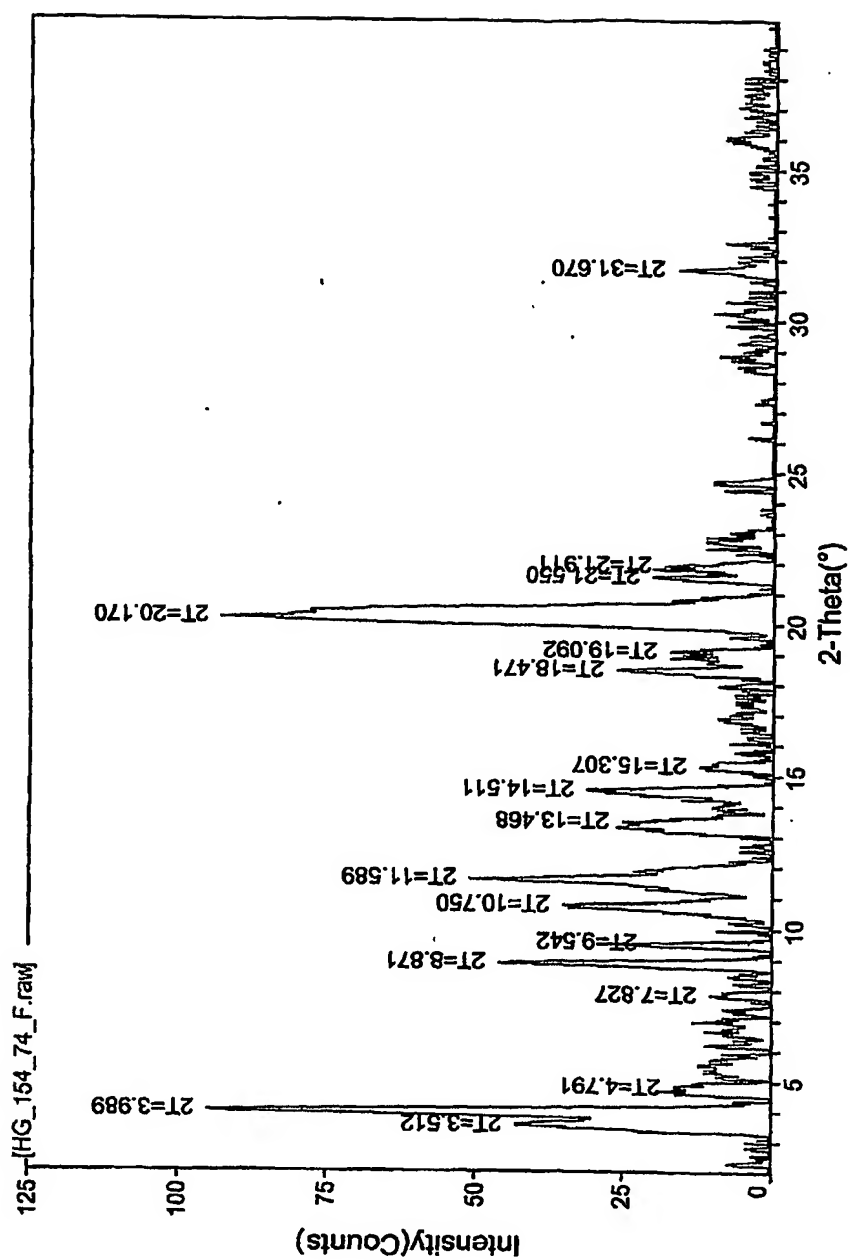


FIG. 53

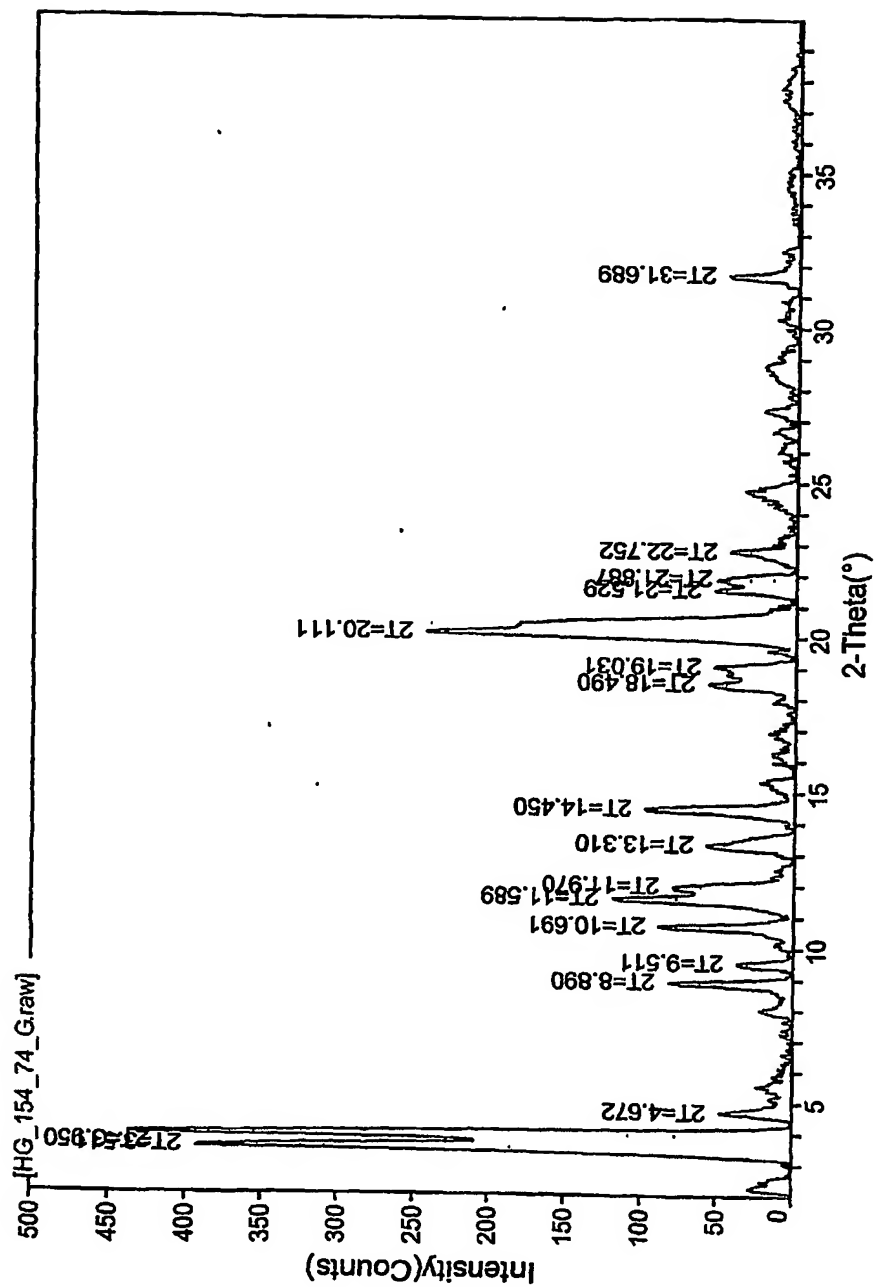


FIG. 54



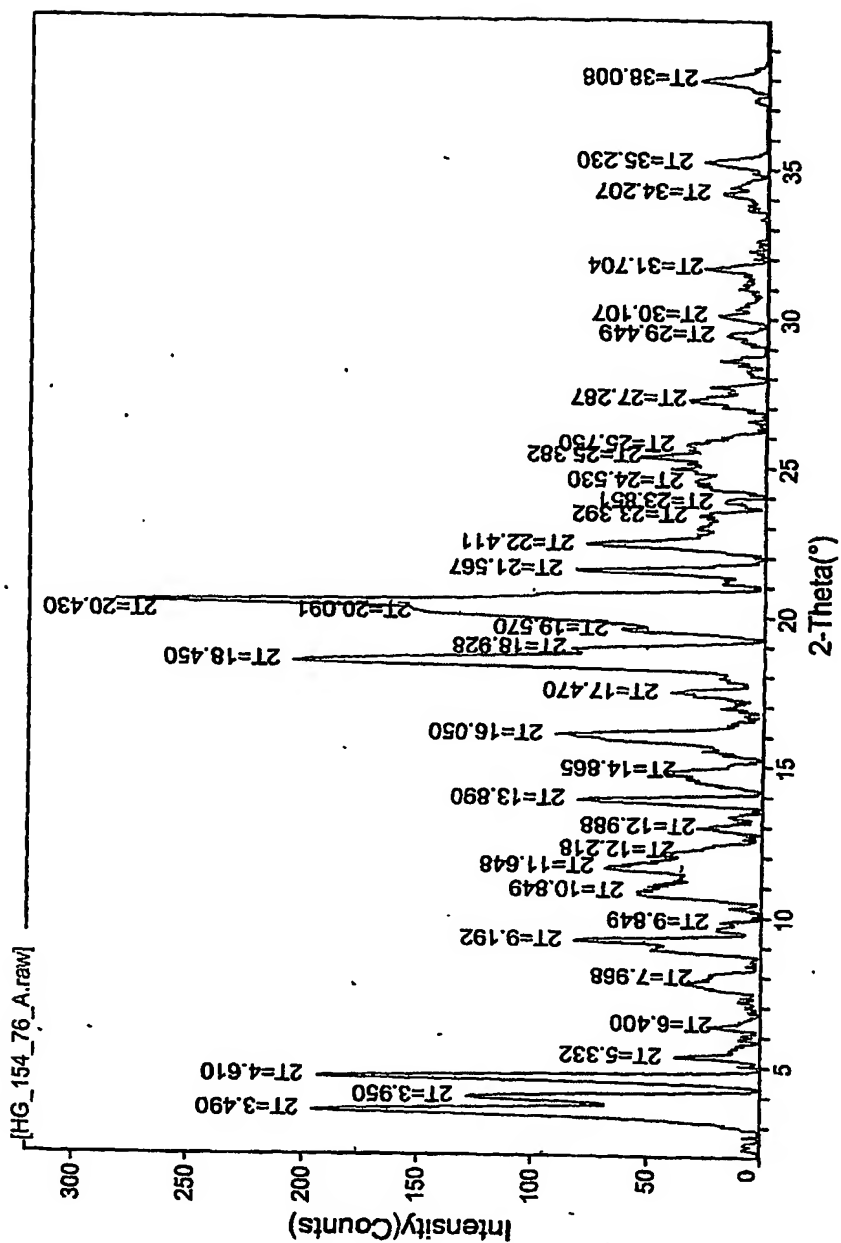


FIG. 55

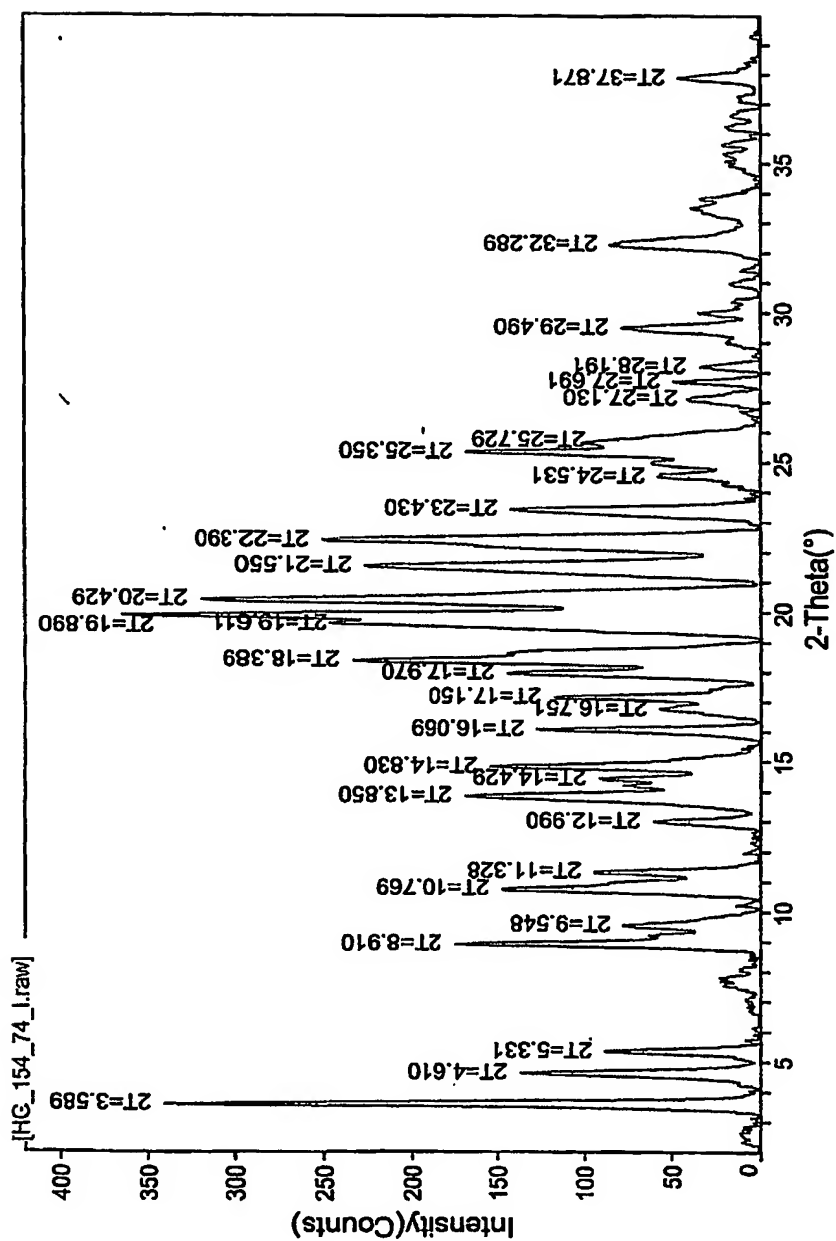


FIG. 56

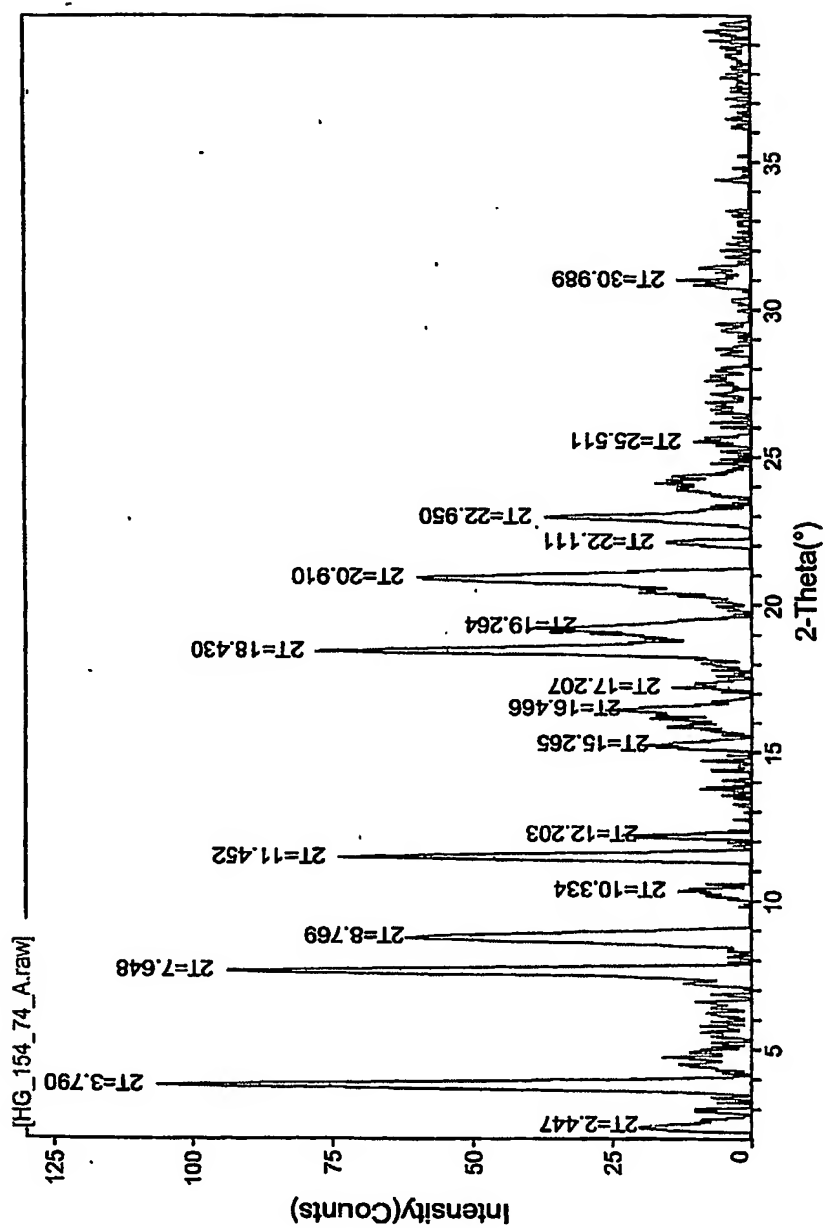


FIG. 57

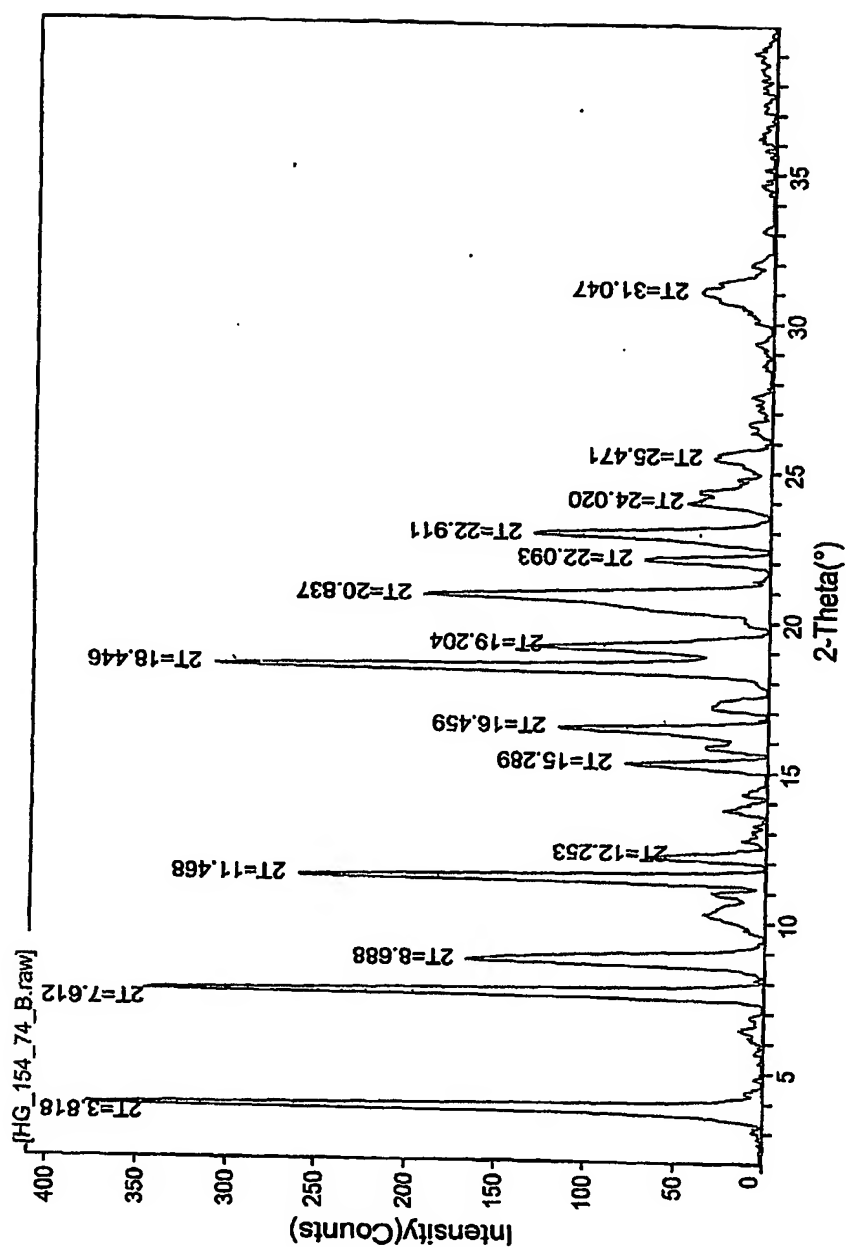


FIG. 58

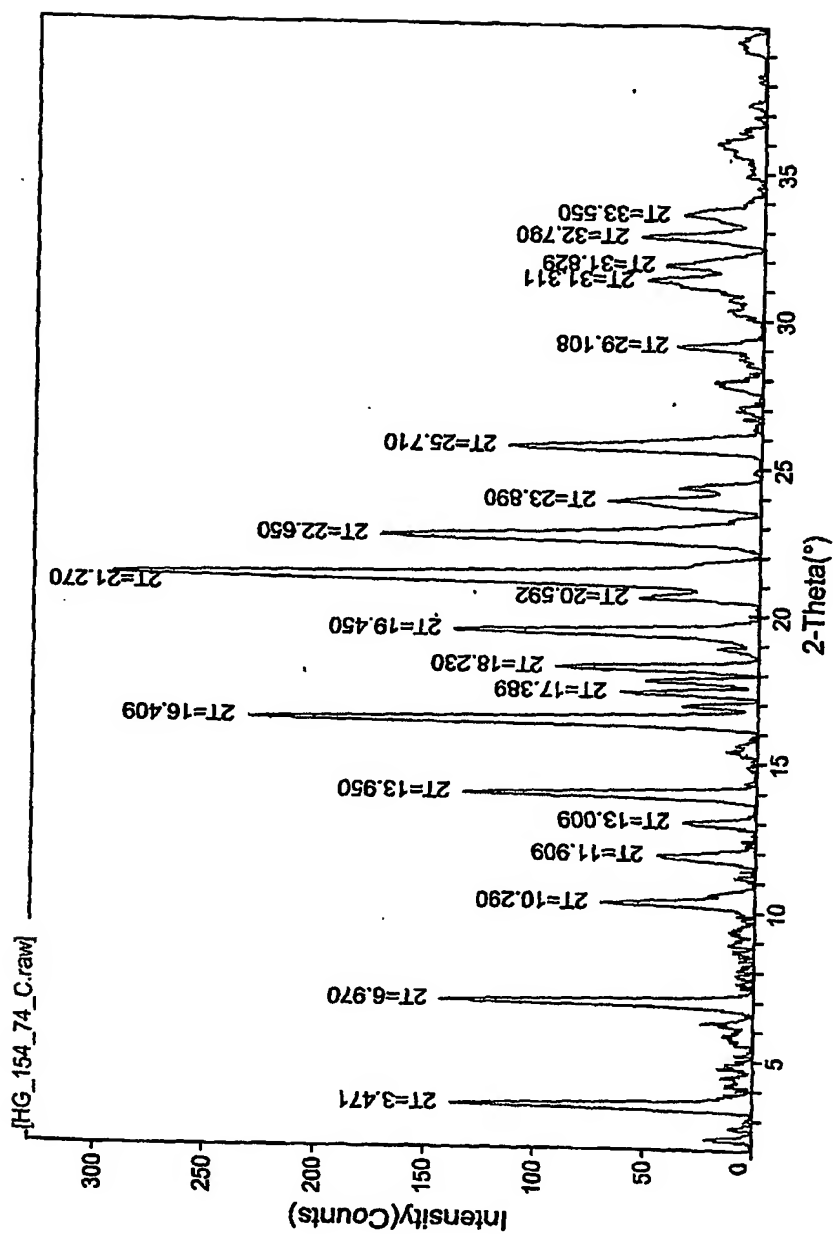


FIG. 59

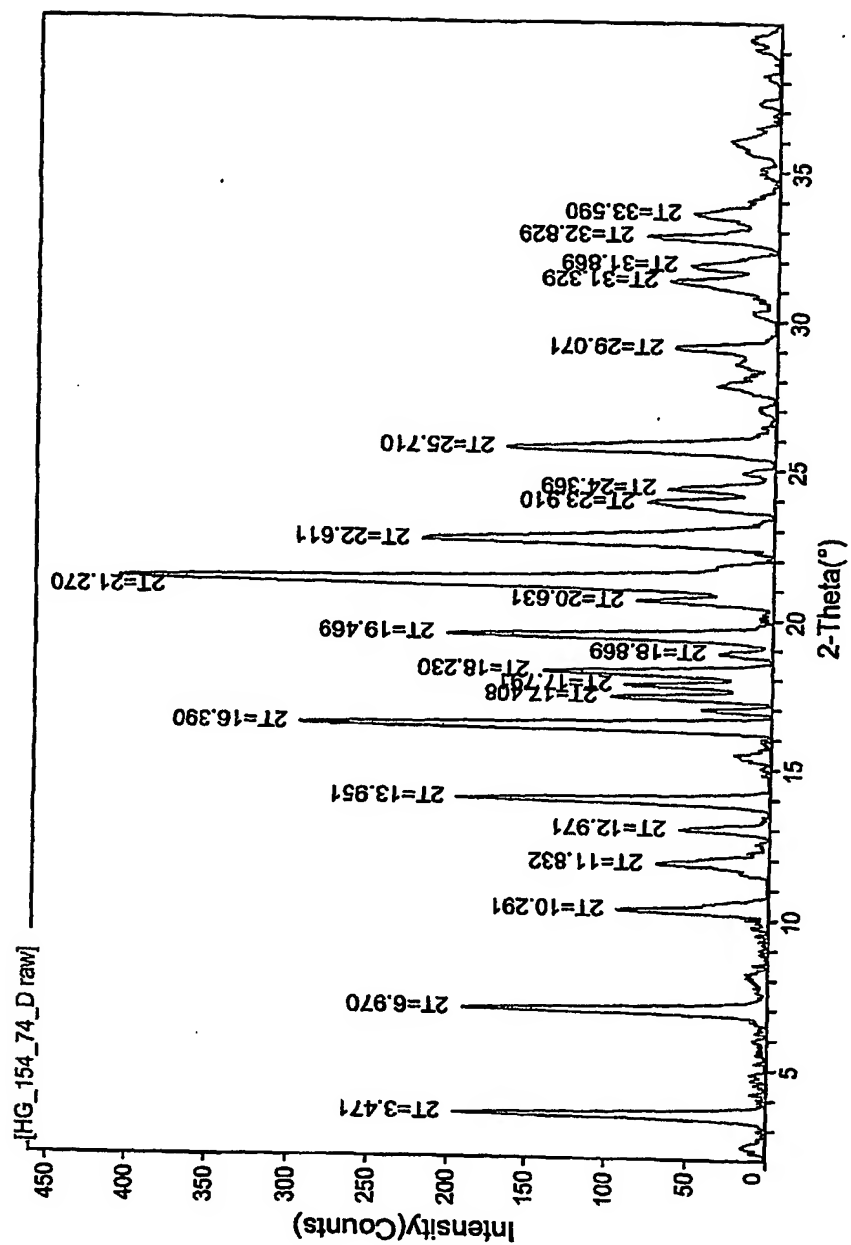


FIG. 60

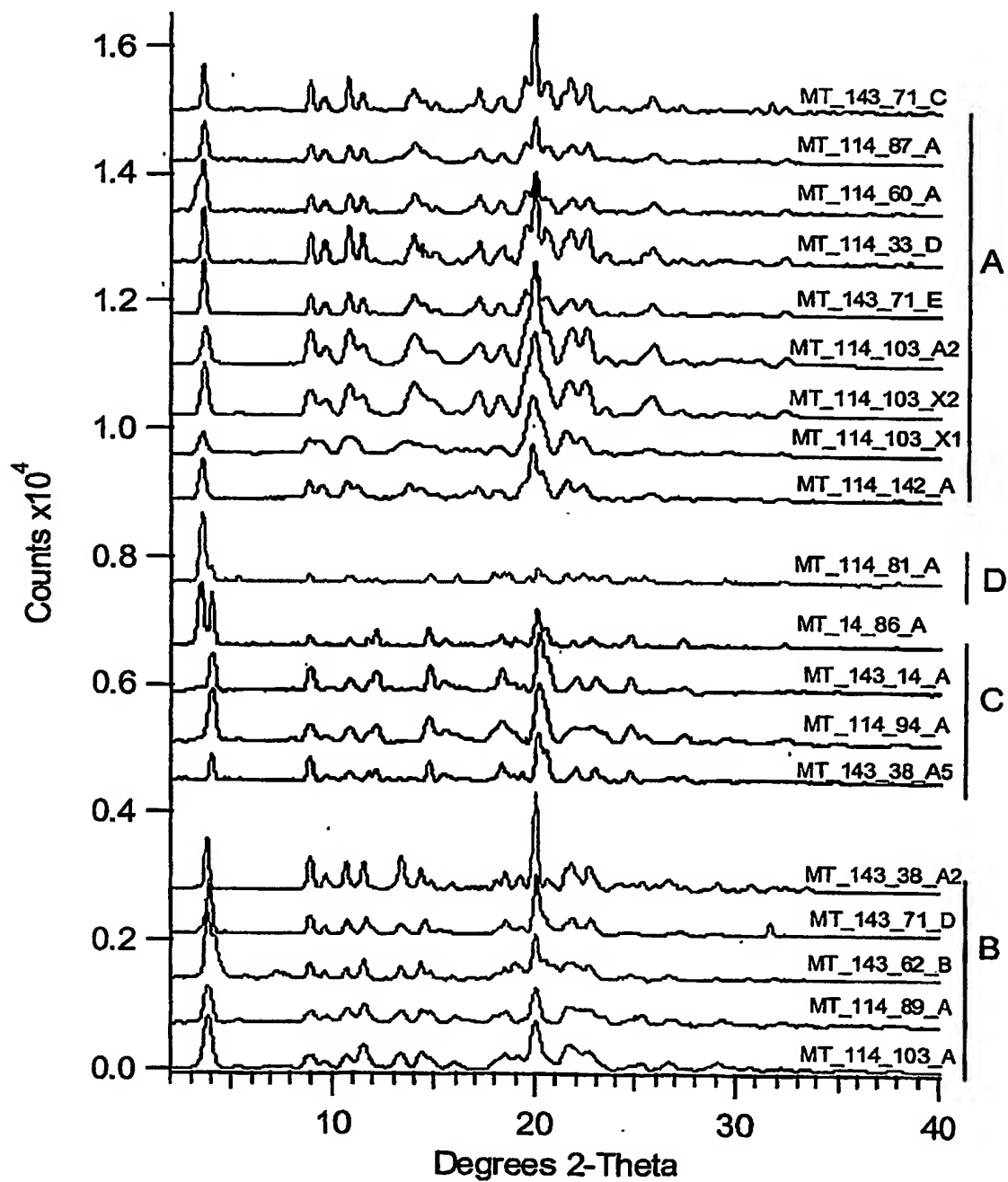


FIG. 61

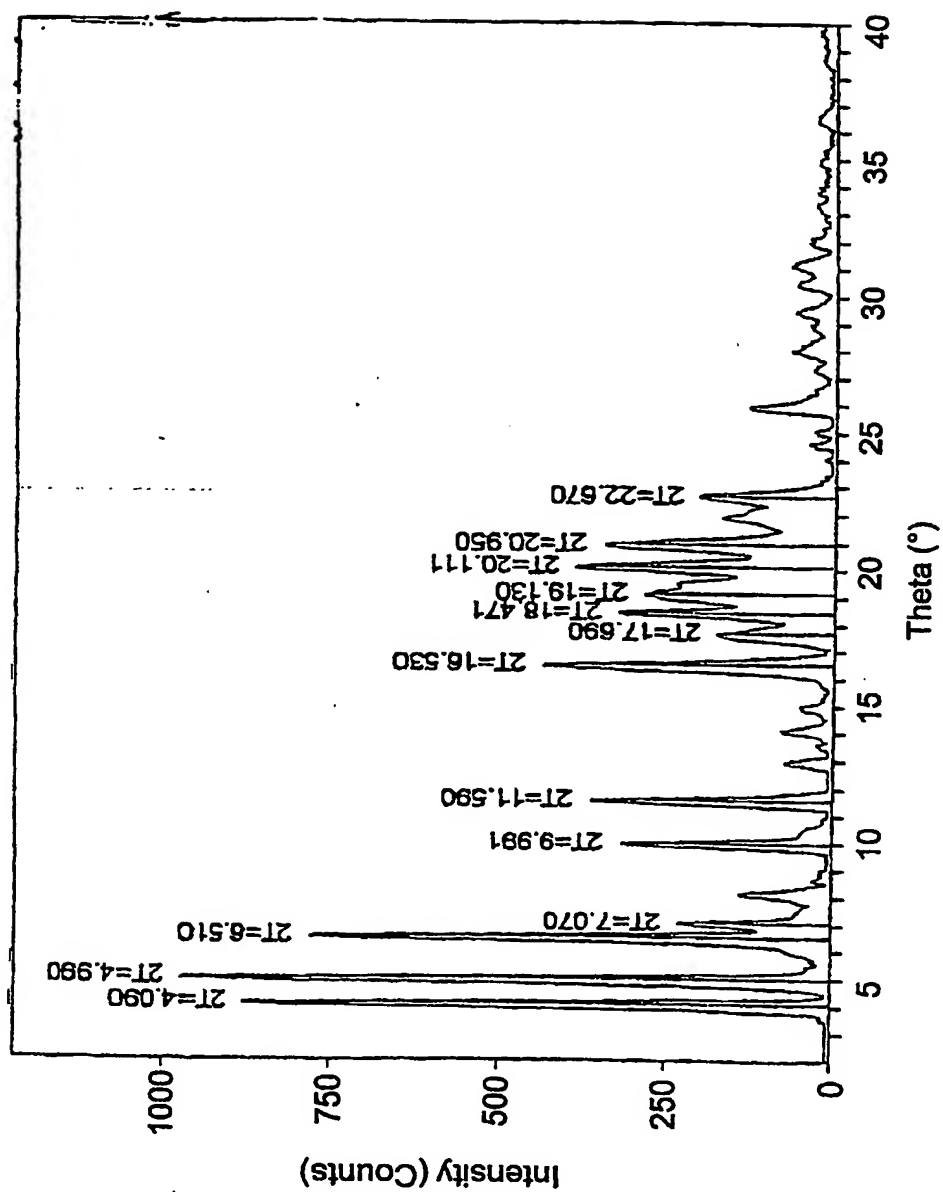


FIG. 62



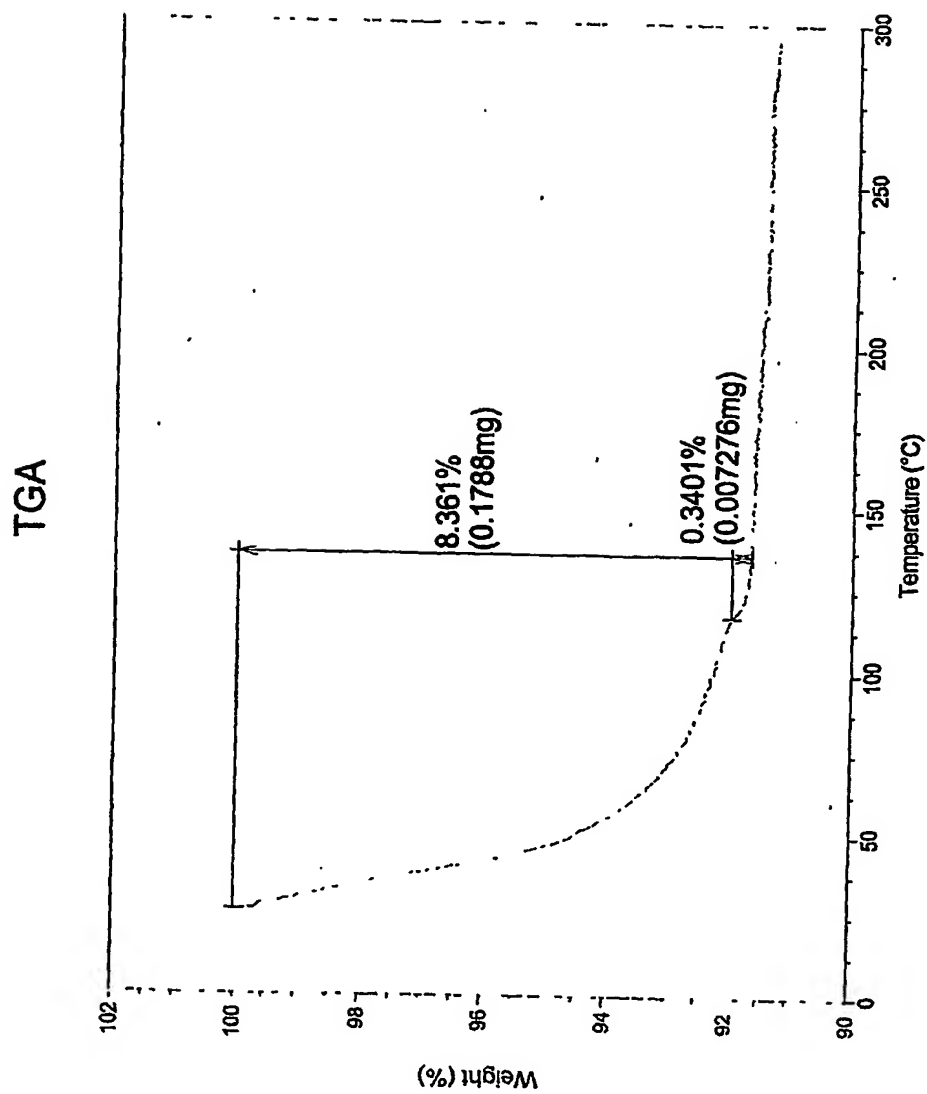


FIG. 63

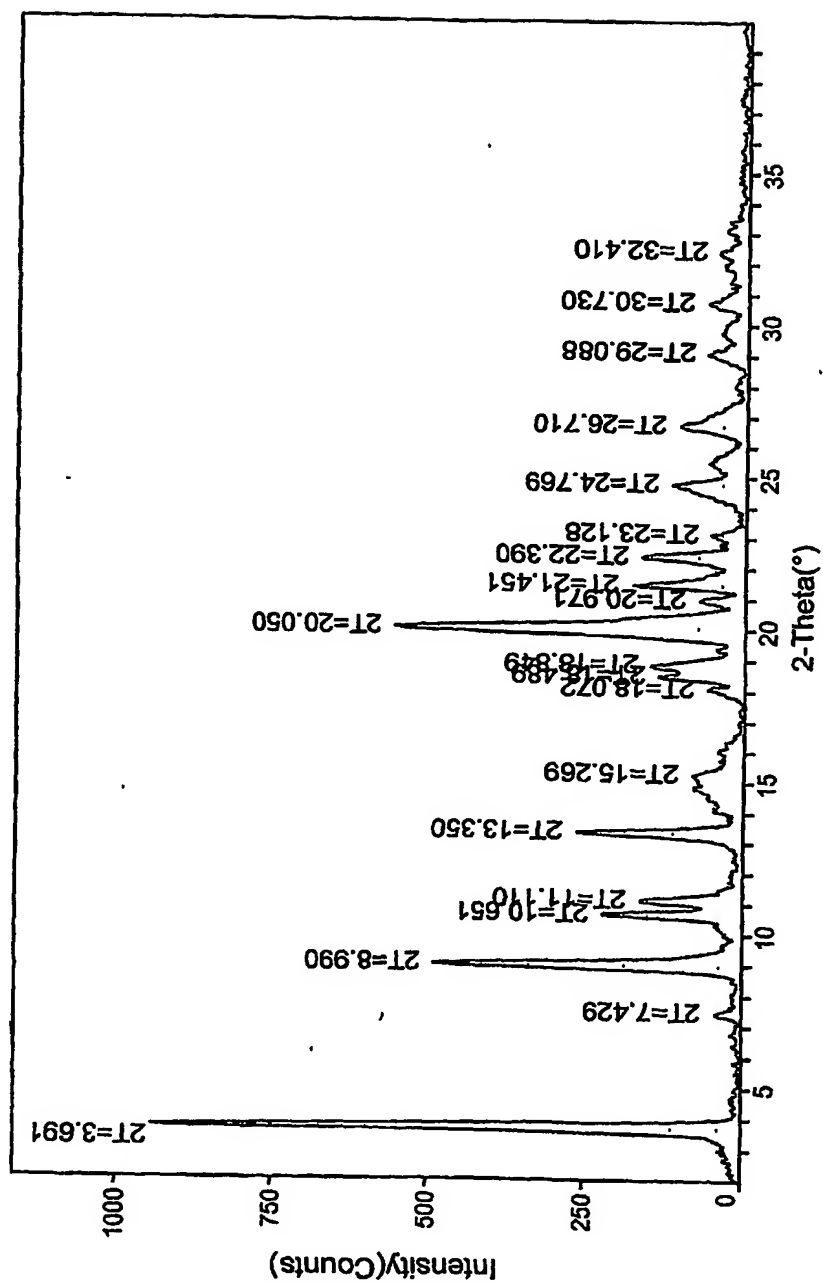


FIG. 64

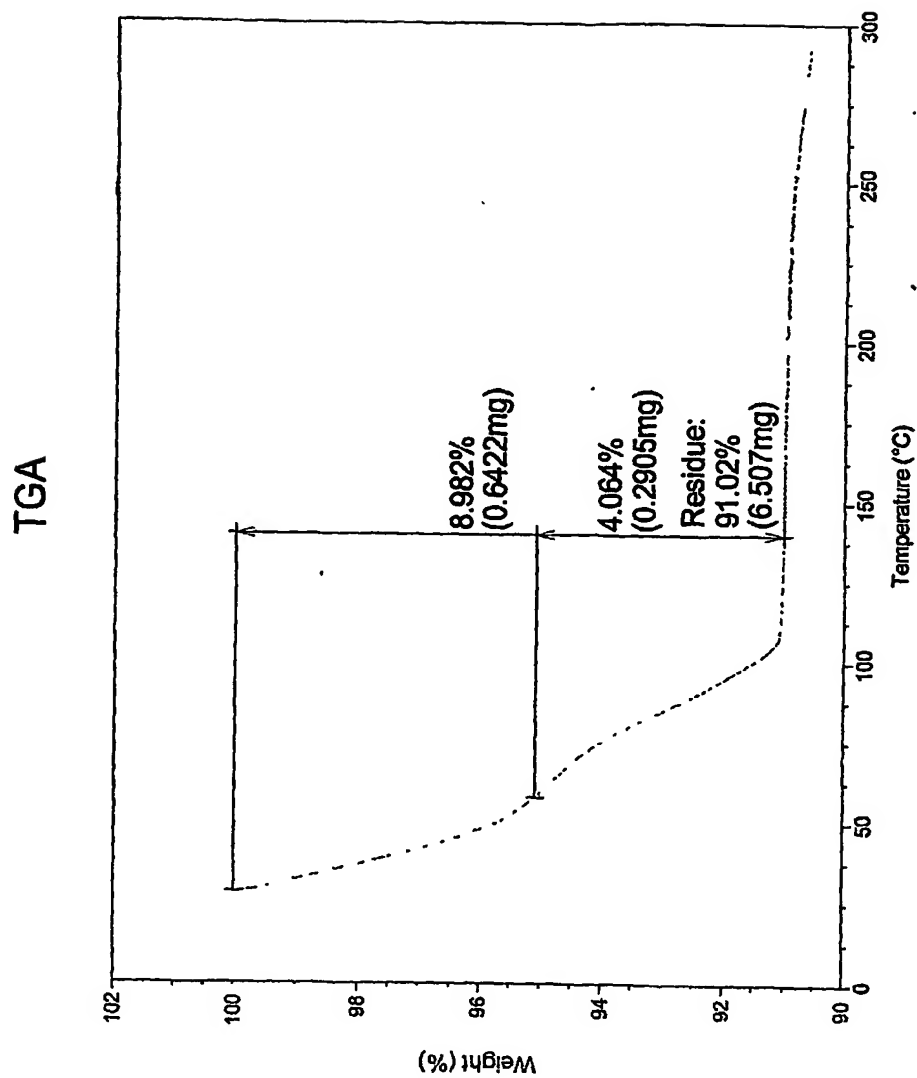


FIG. 65

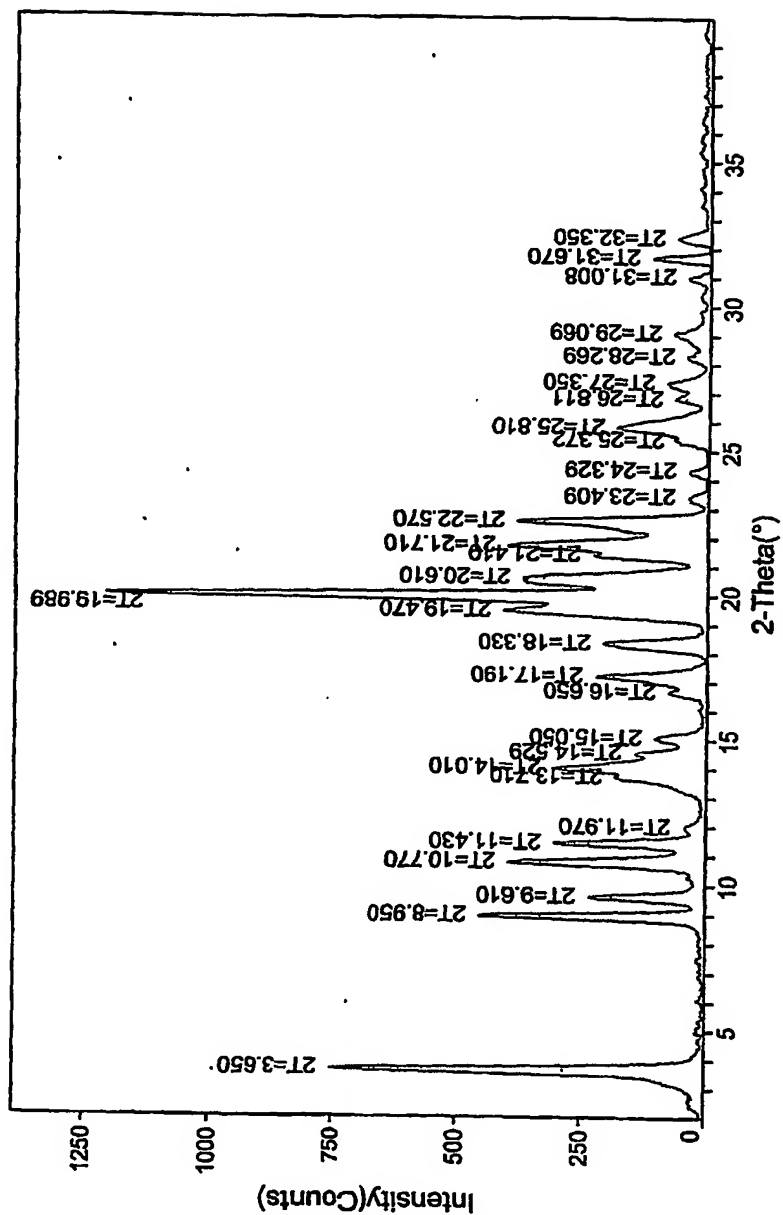


FIG. 66

Comparison of celecoxib formulations: fresh preparation and 22 weeks at 40°C

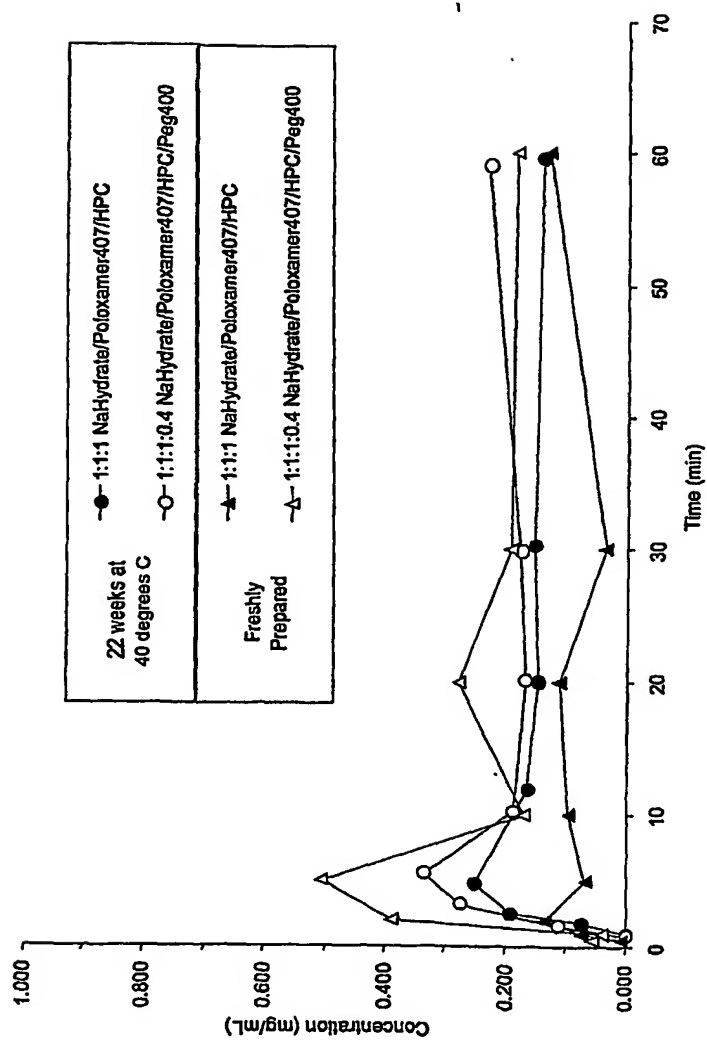


FIG. 67

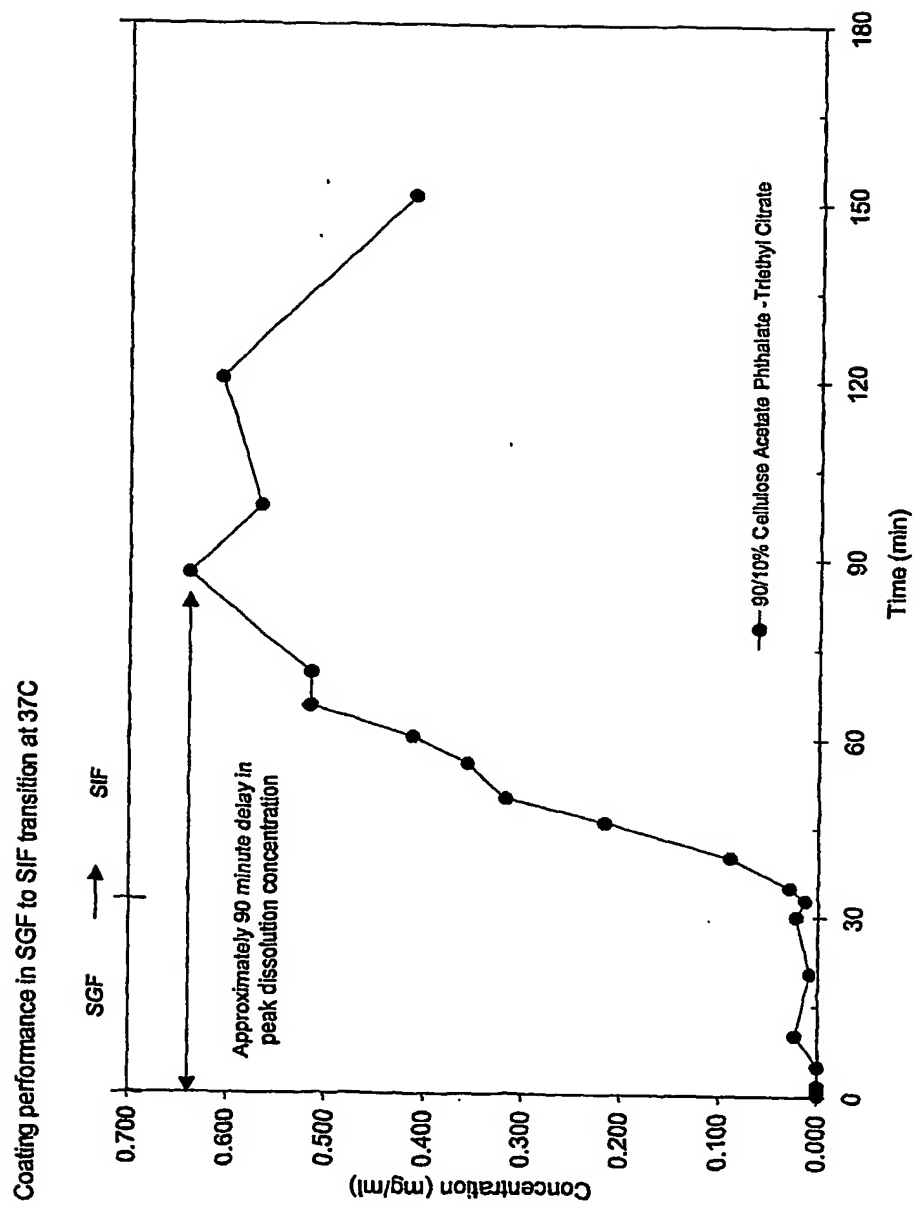


FIG. 68

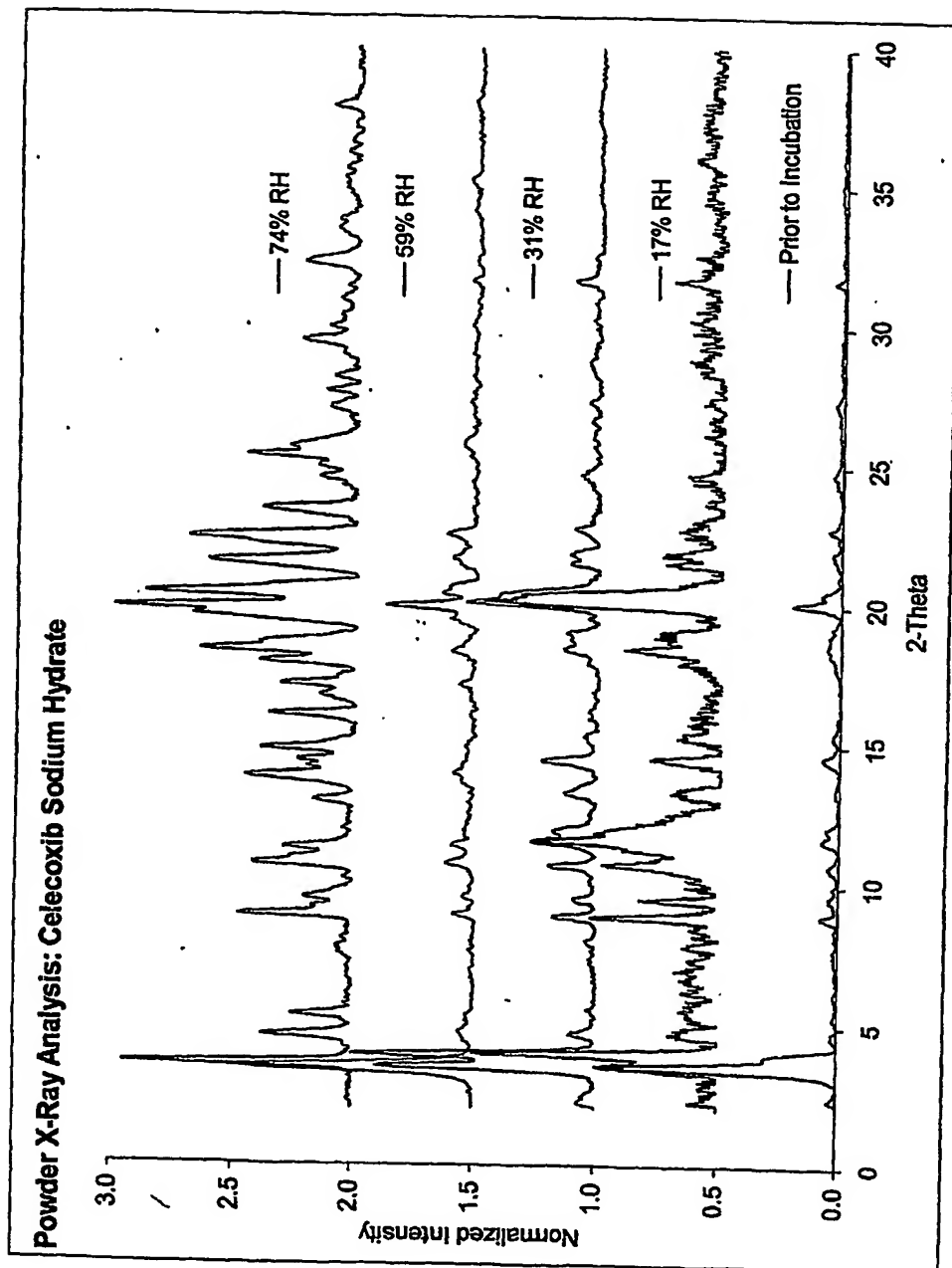


FIG. 69

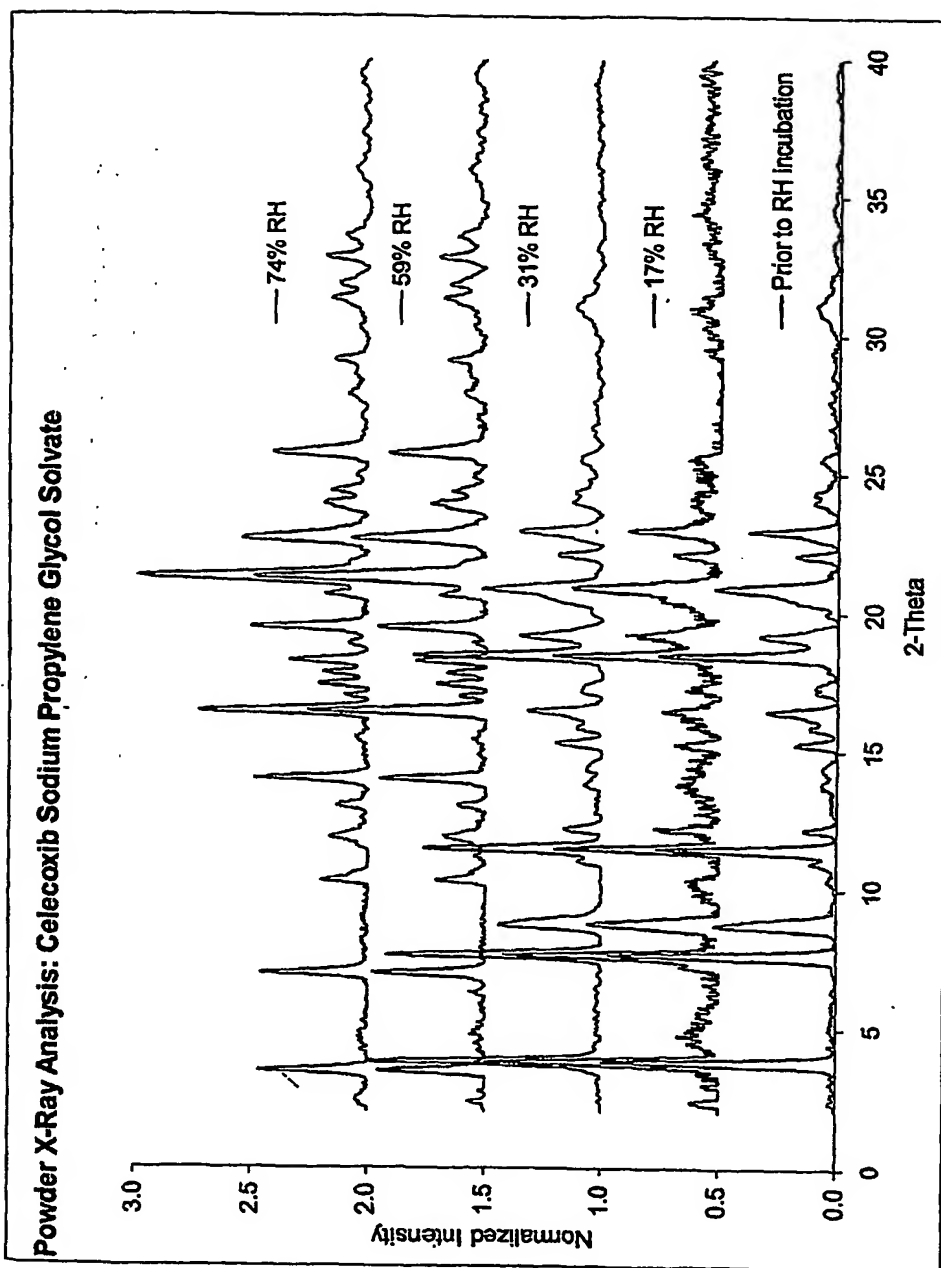


FIG. 70



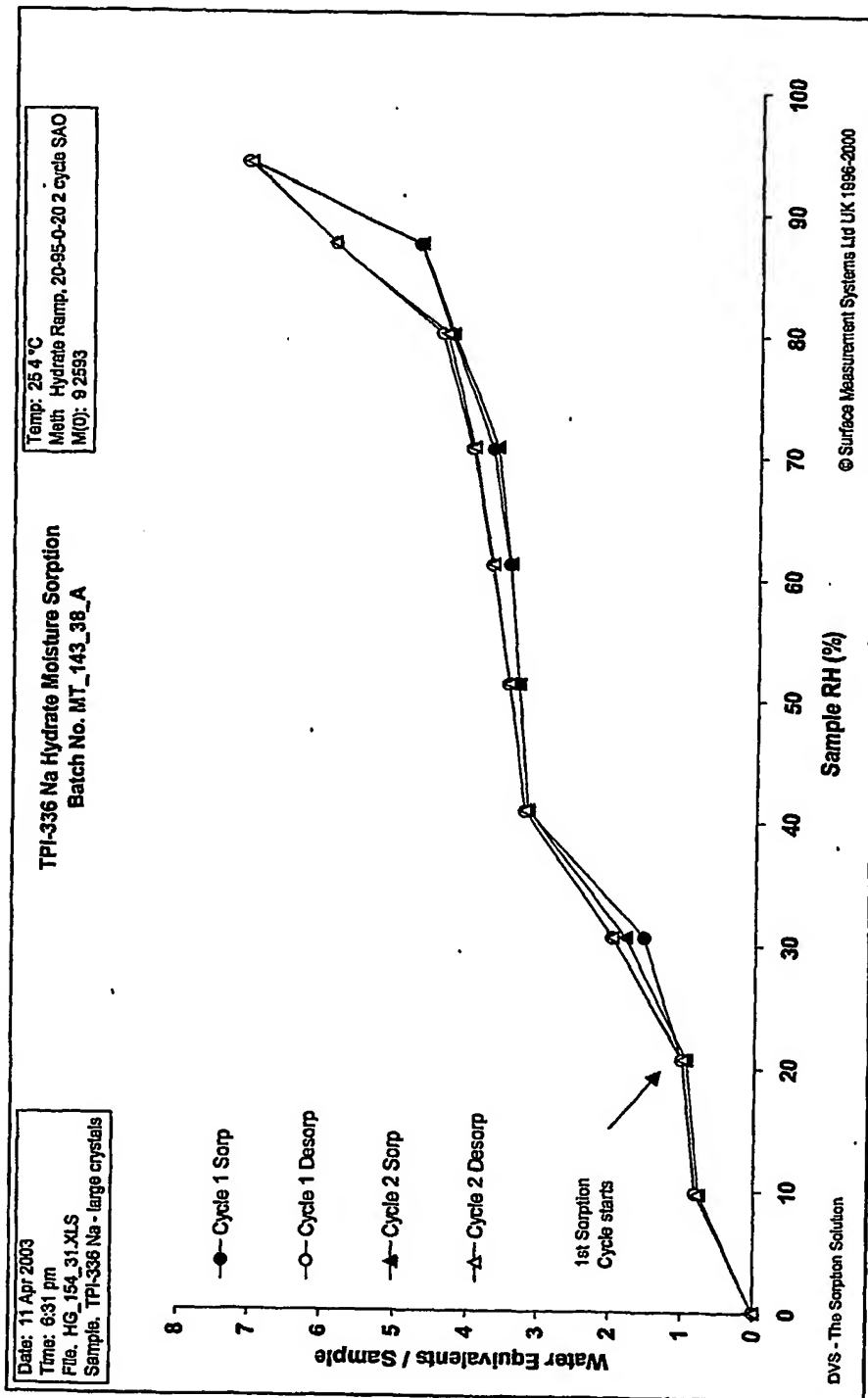


FIG. 71

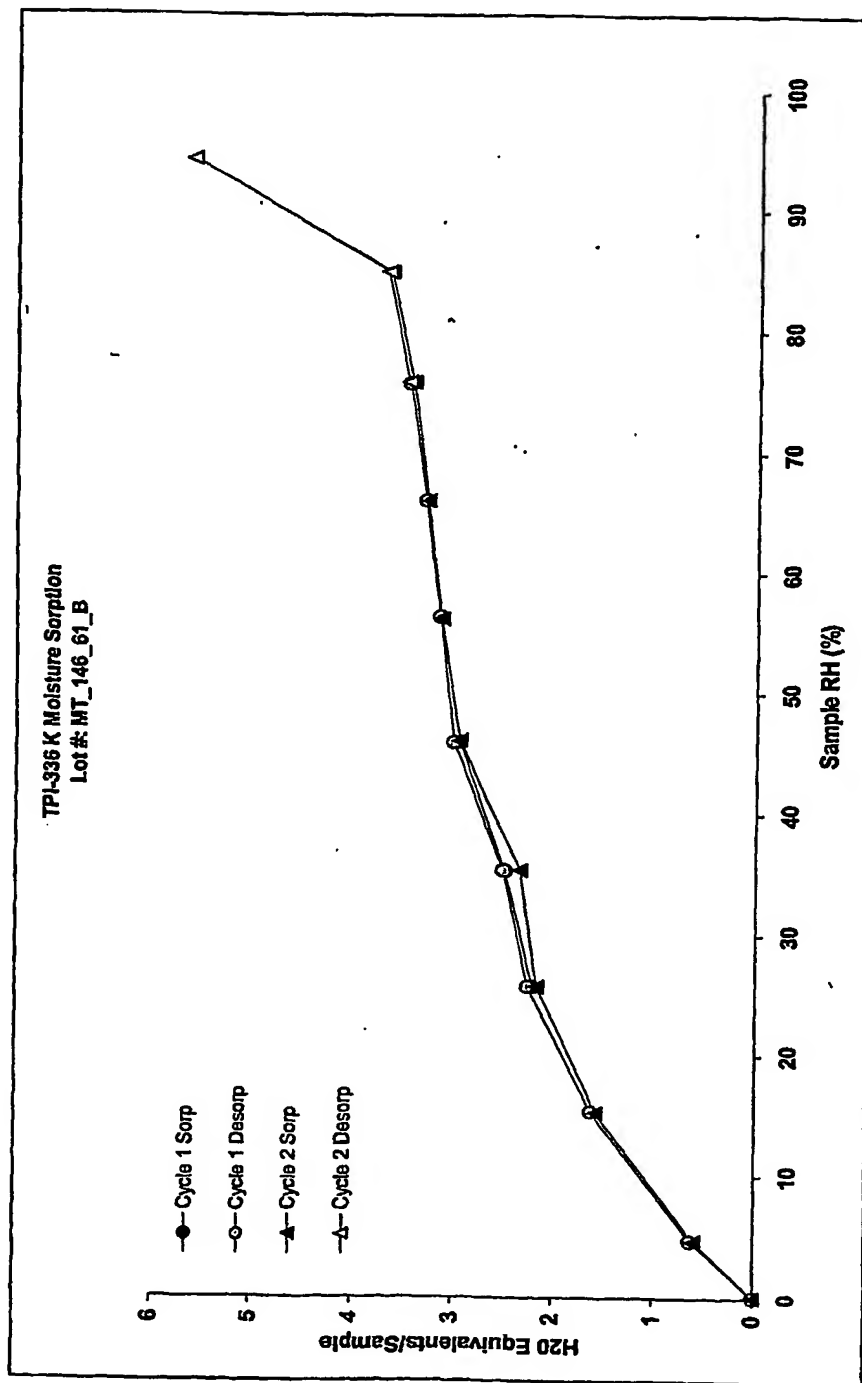


FIG. 72A

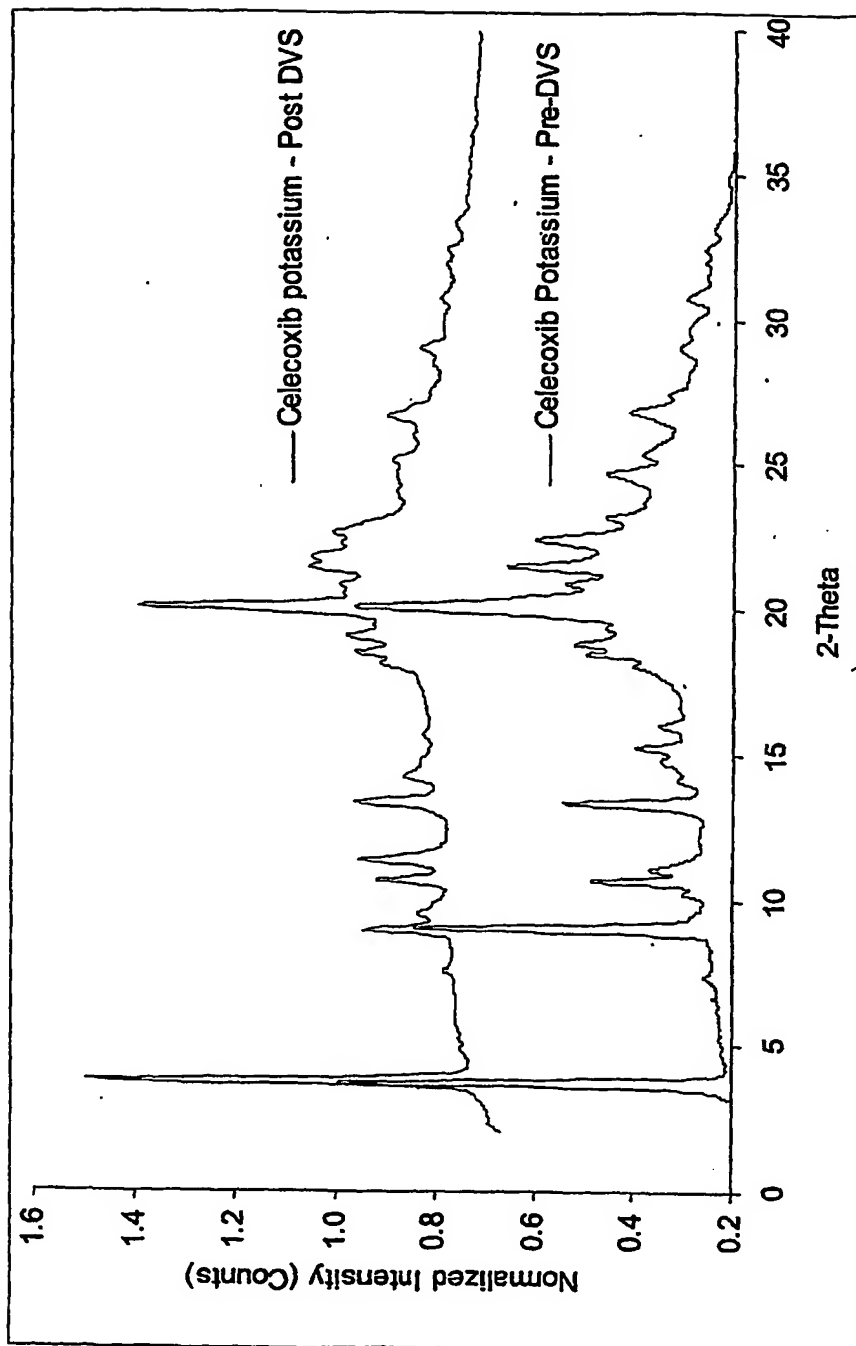


FIG. 72B

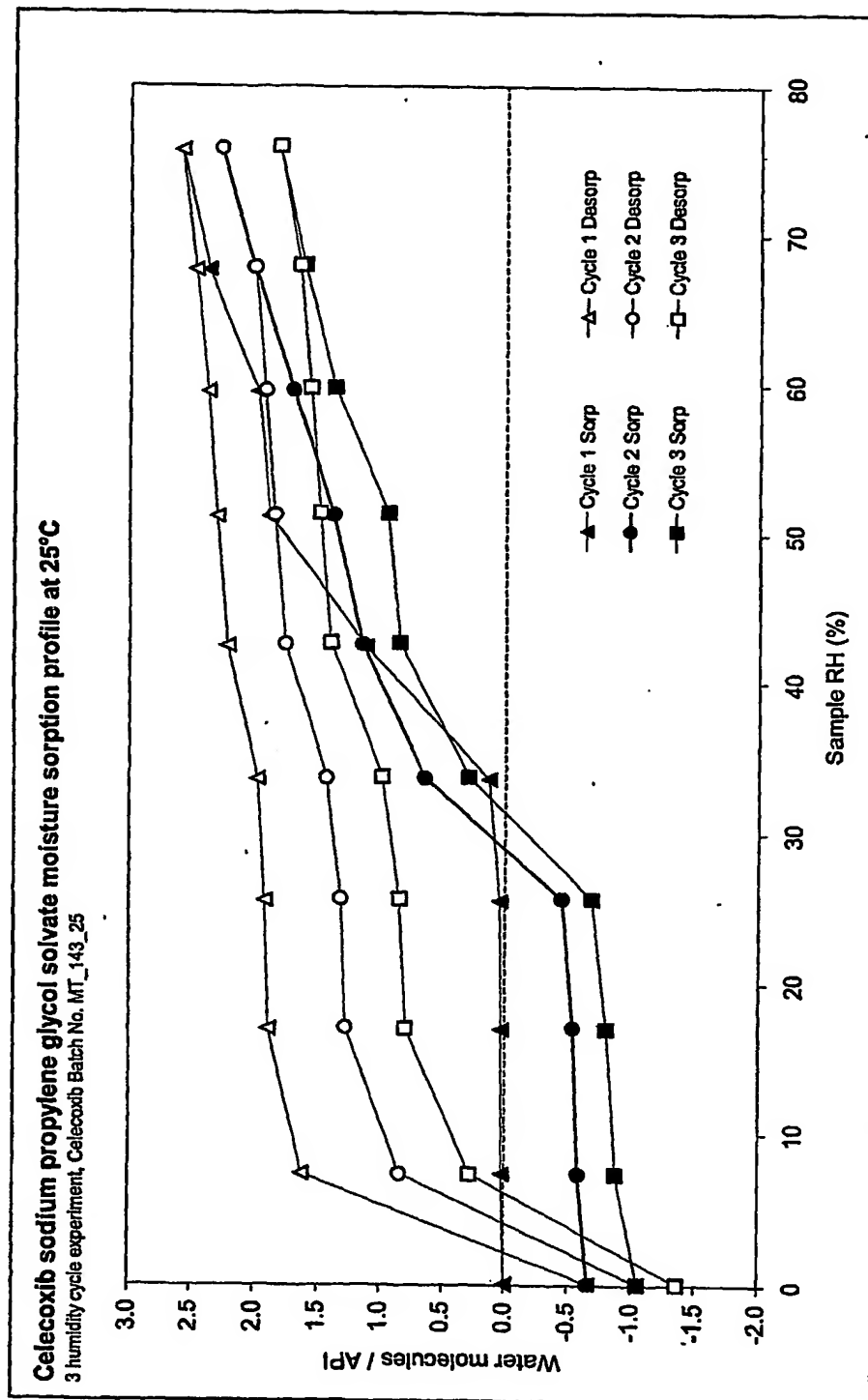
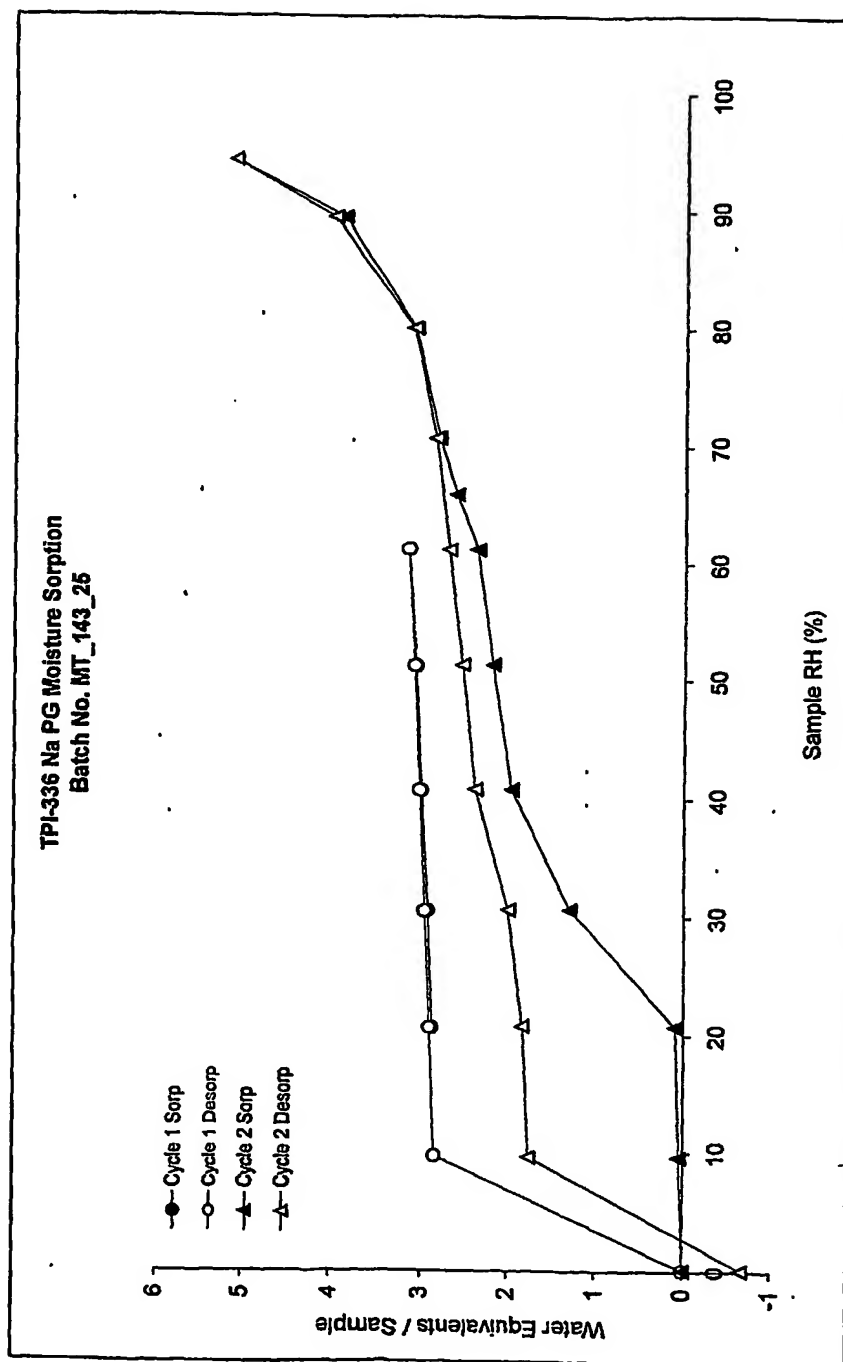


FIG. 73



**FIG. 74**

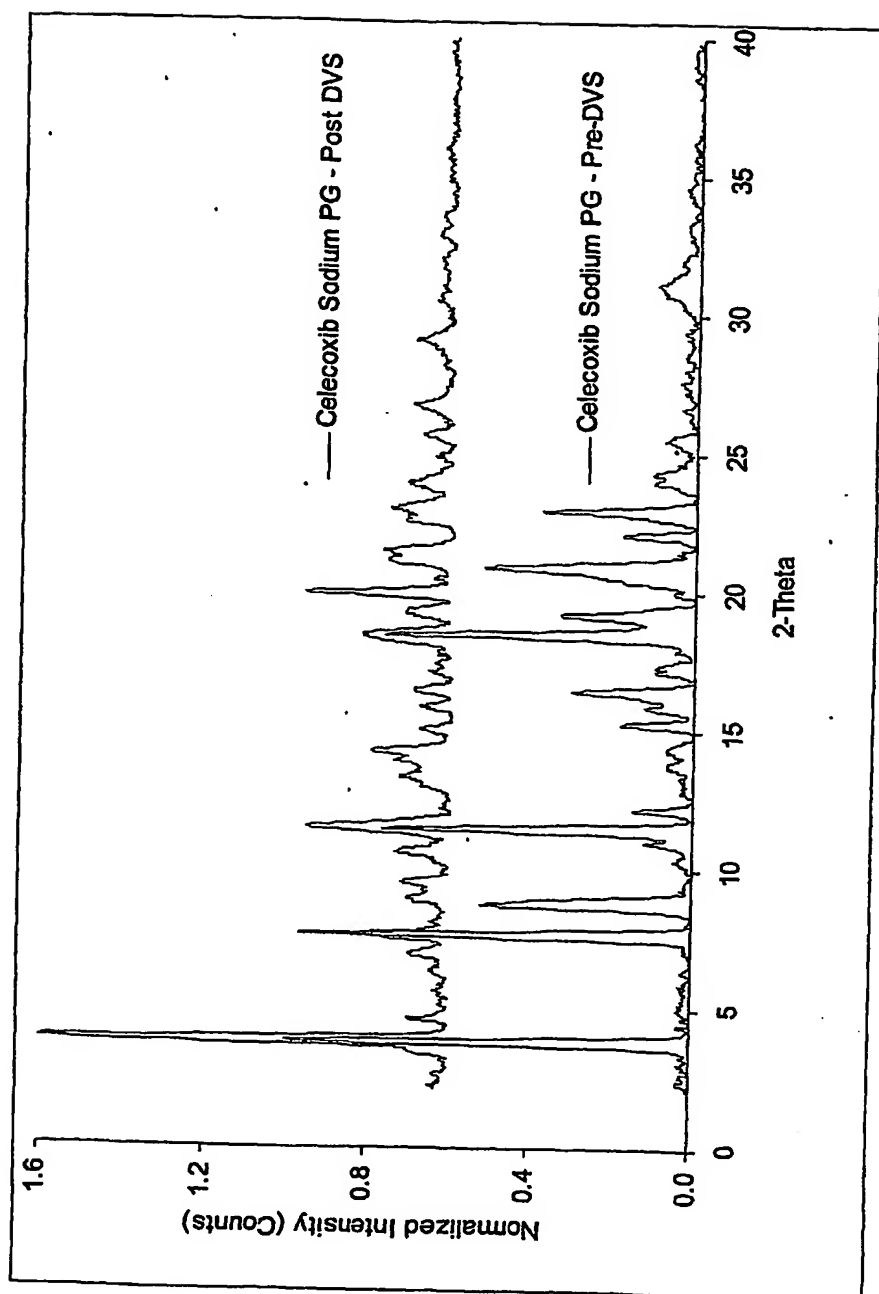


FIG. 75

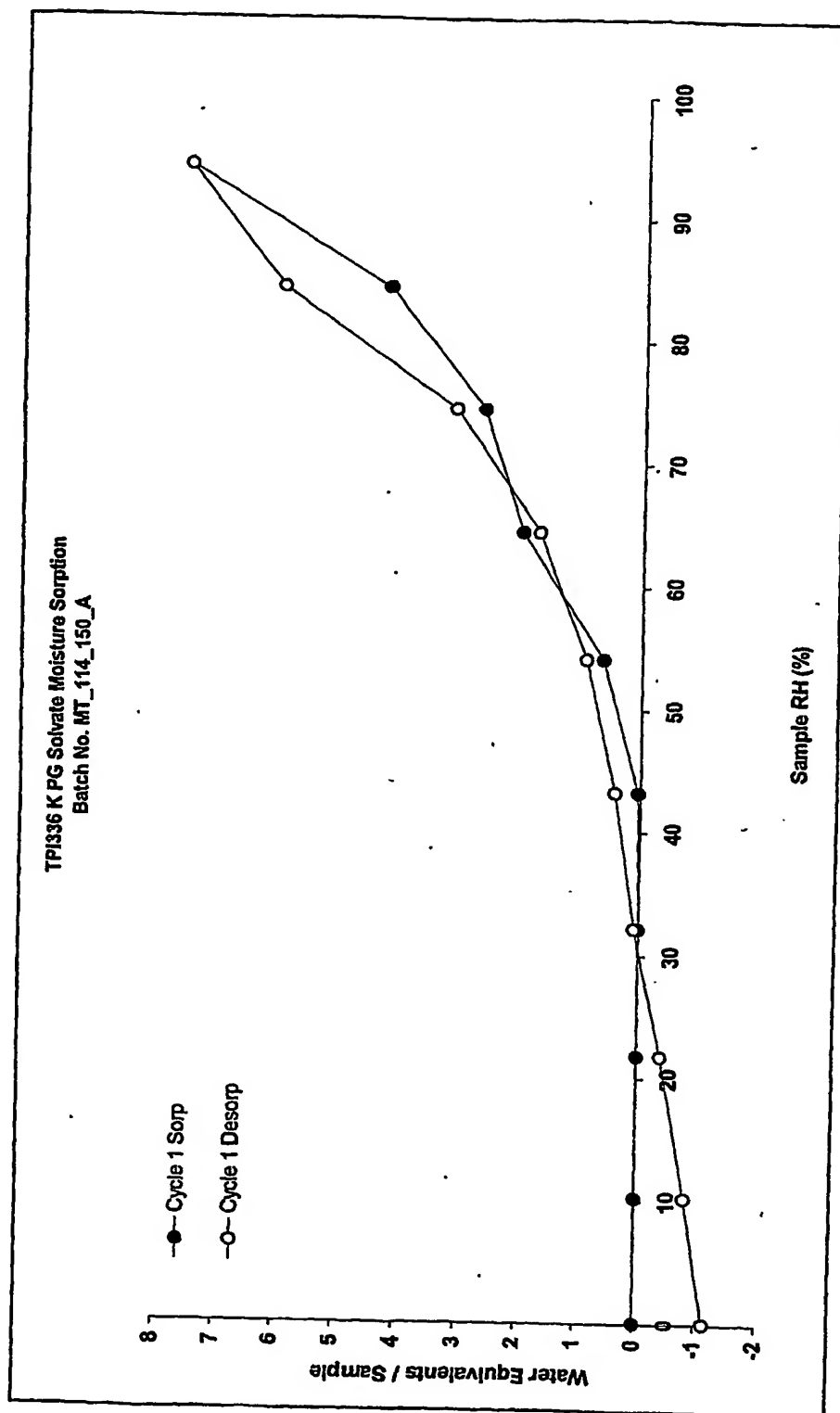


FIG. 76

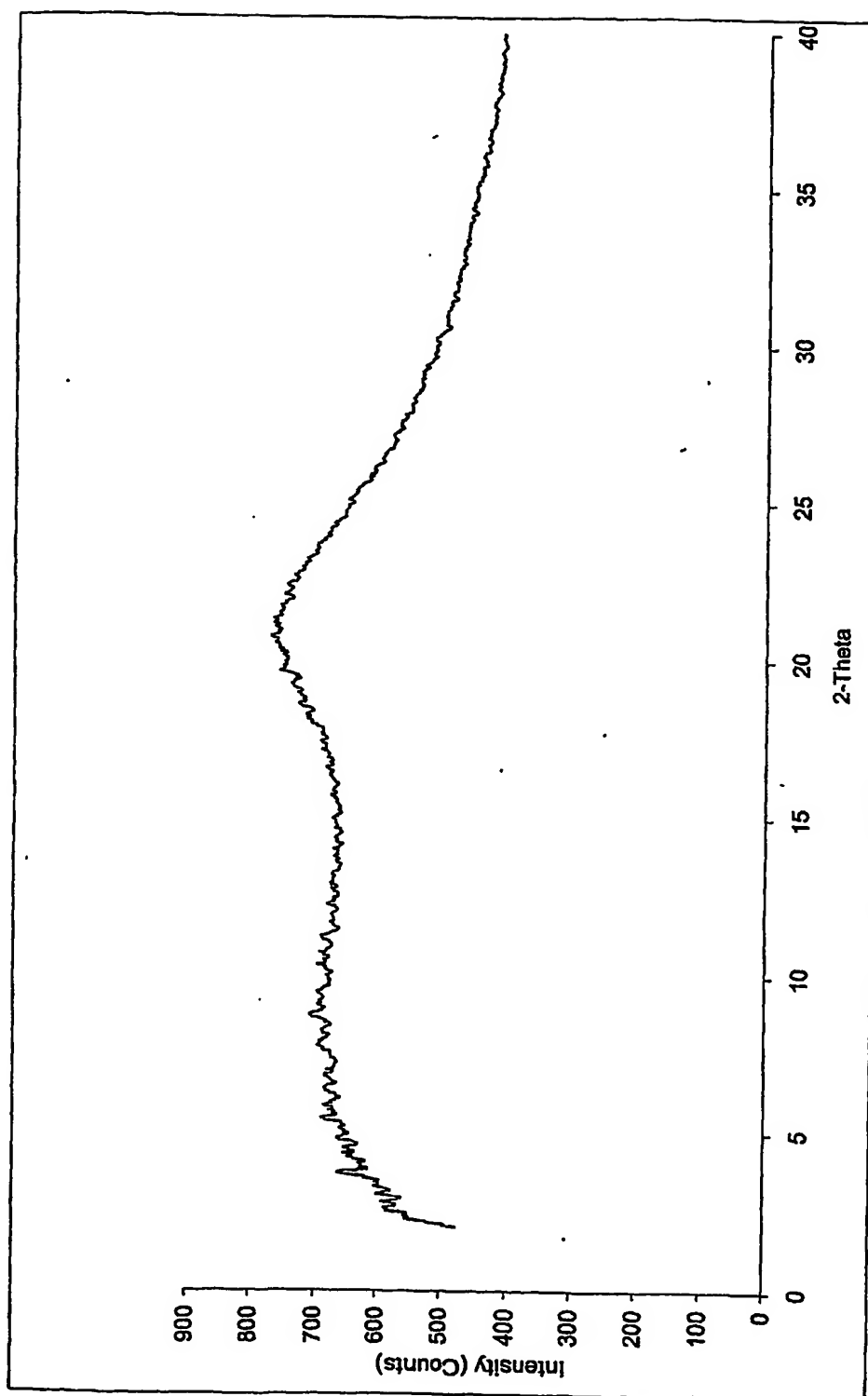
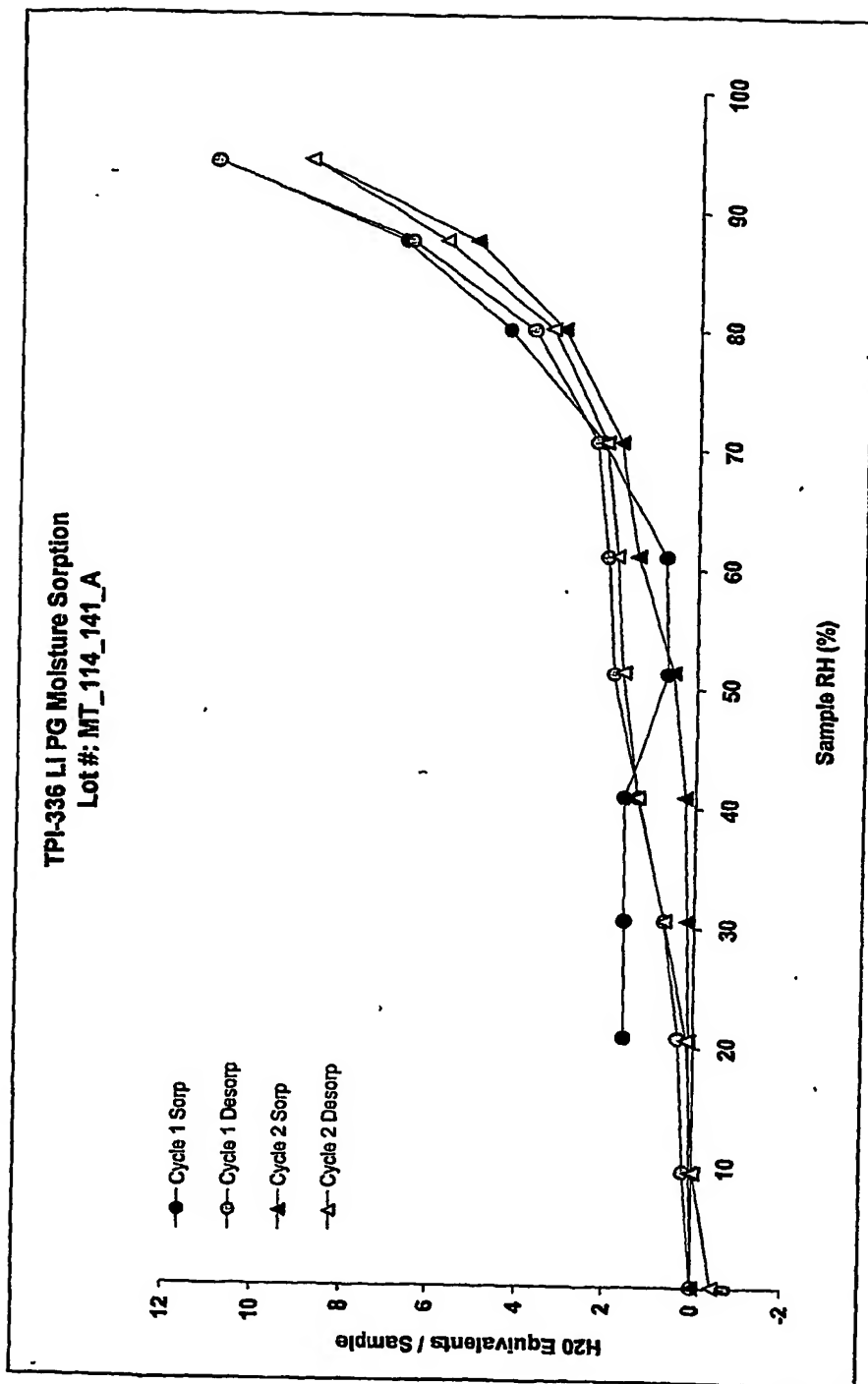


FIG. 77





**FIG. 78**

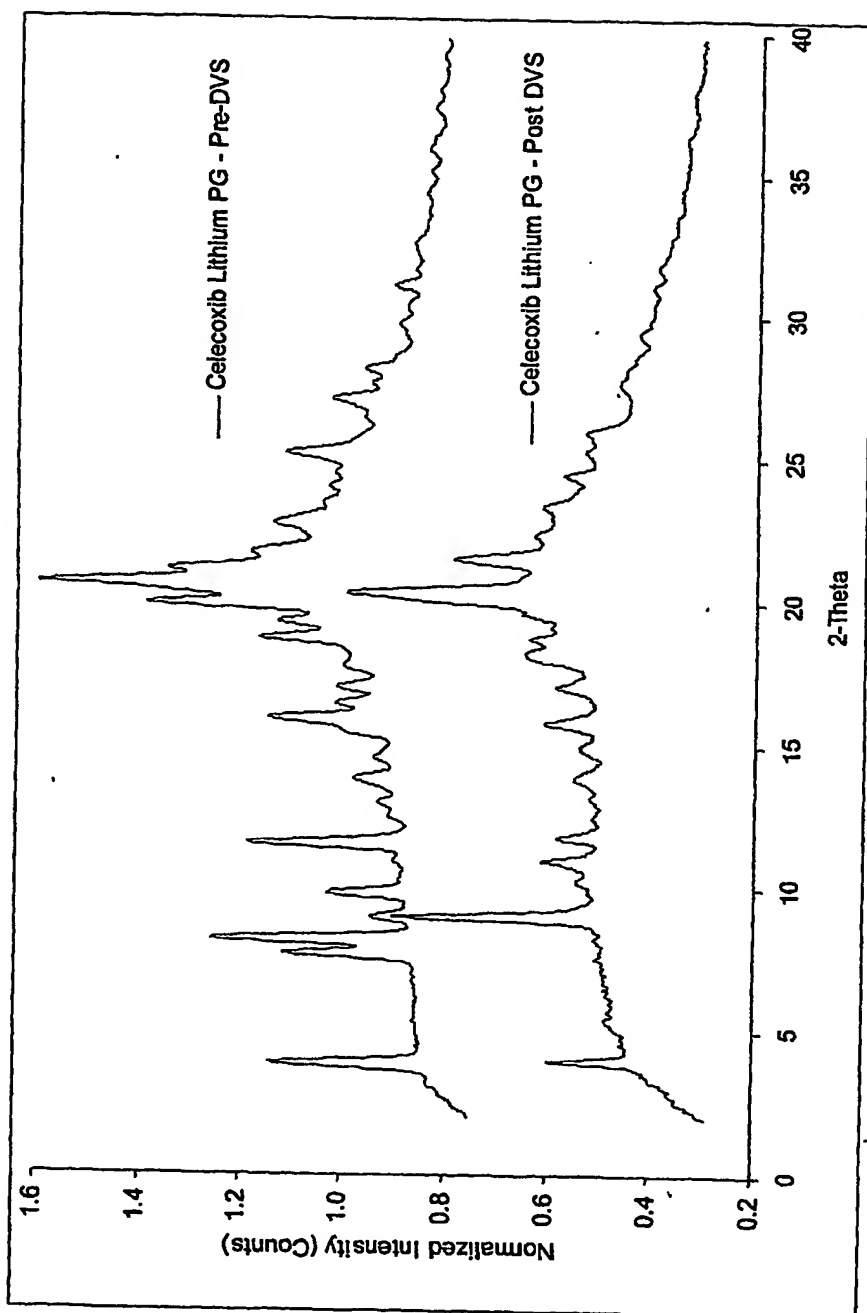
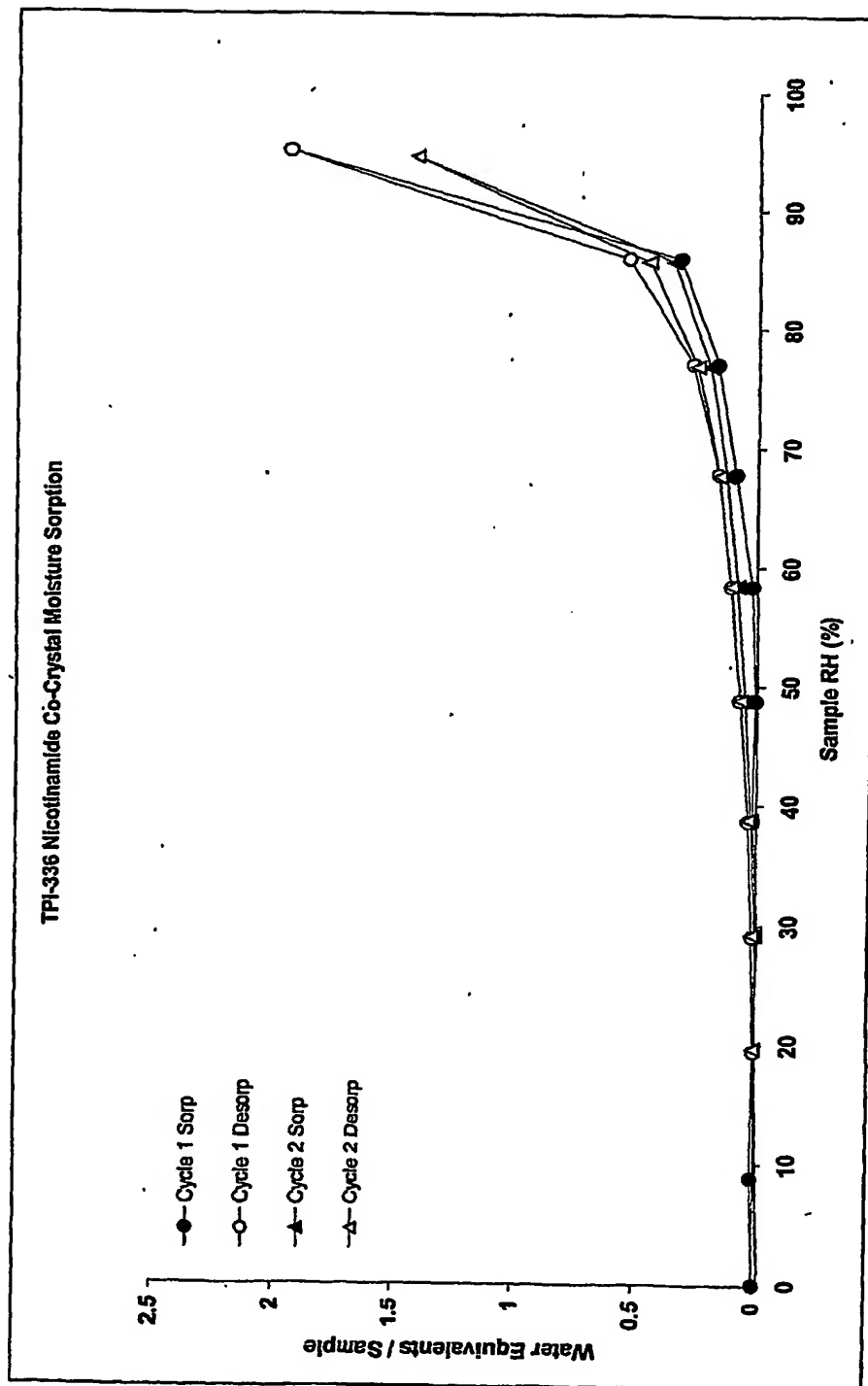


FIG. 79

**FIG. 80**

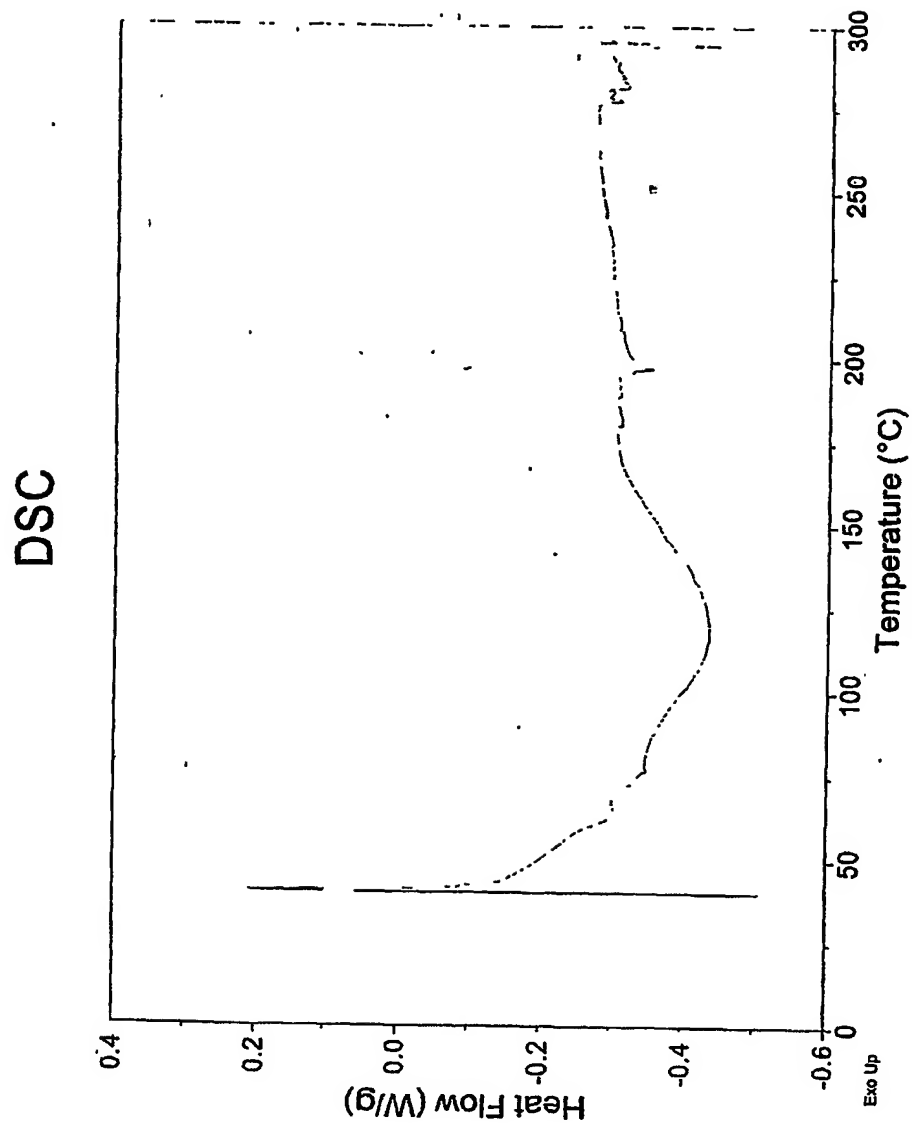


FIG. 81

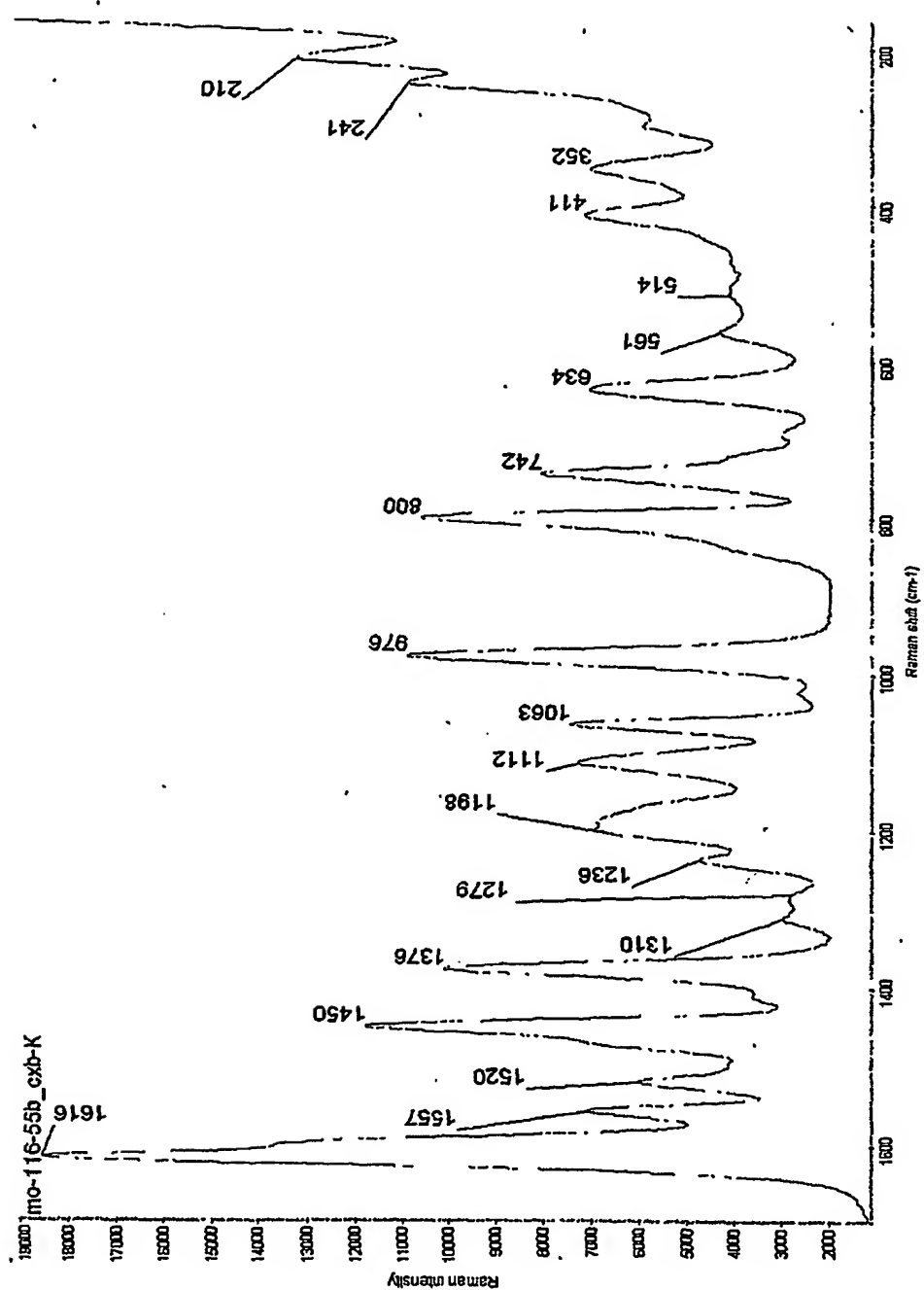


FIG. 82

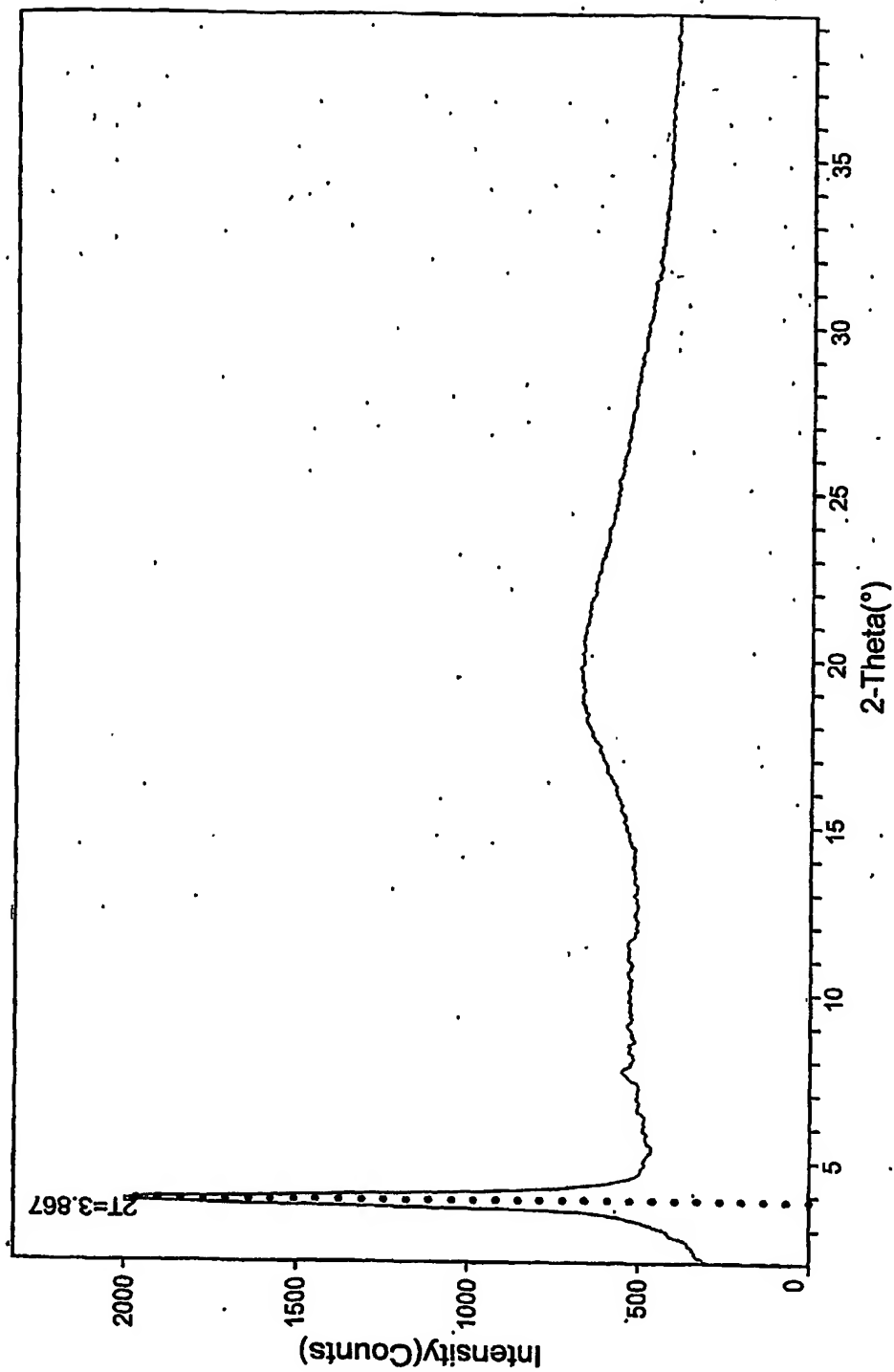


FIG. 83

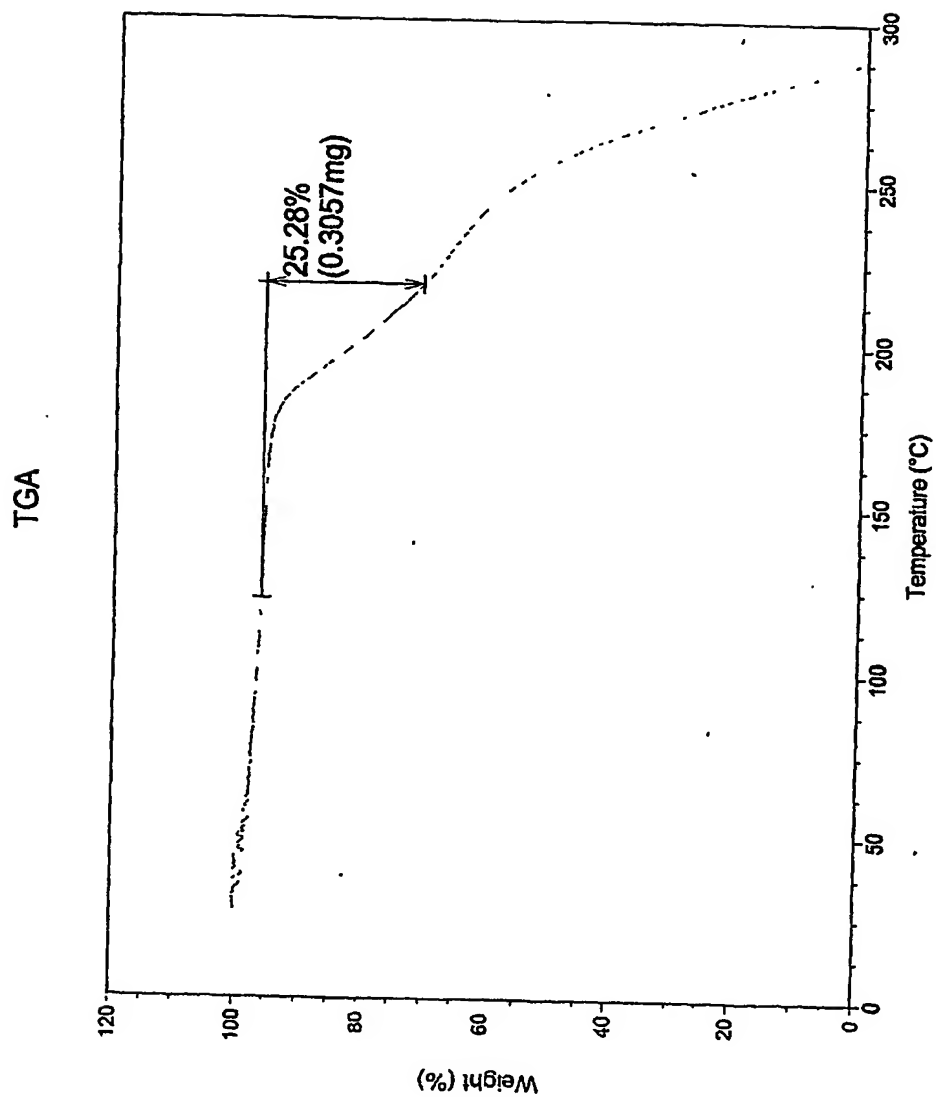


FIG. 84

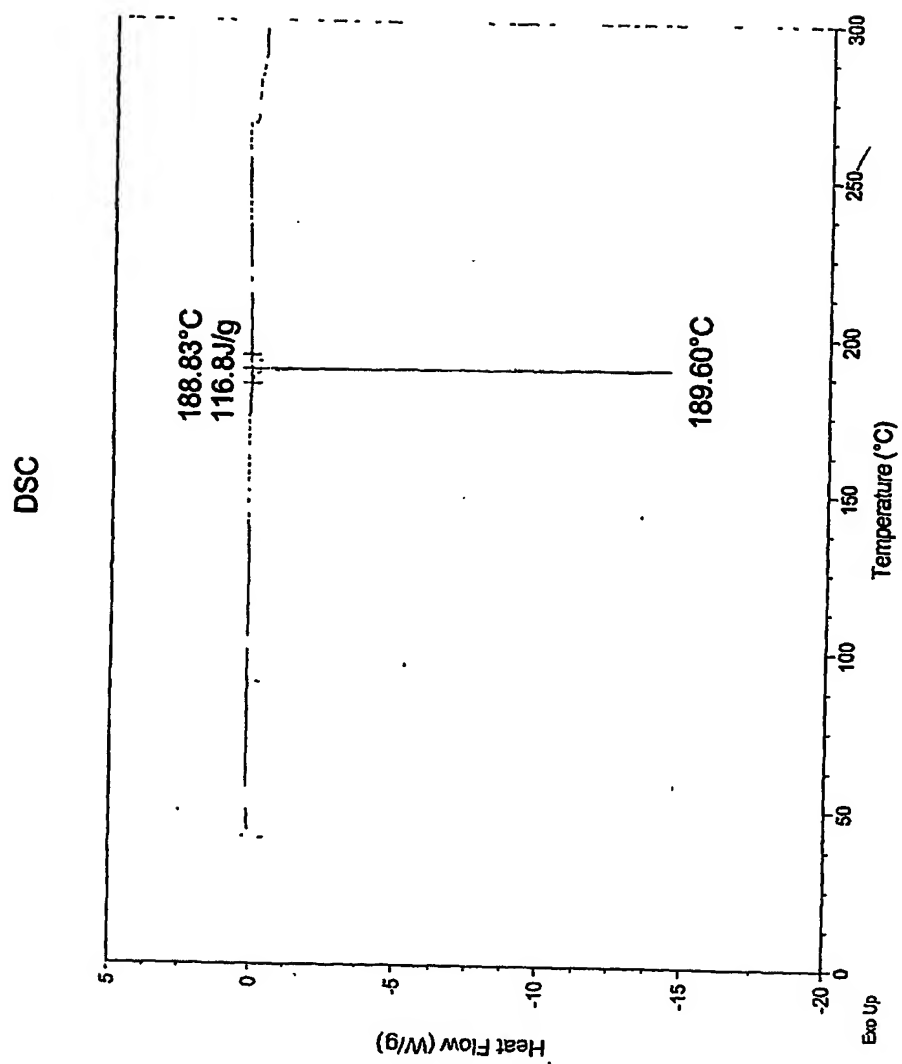


FIG. 85



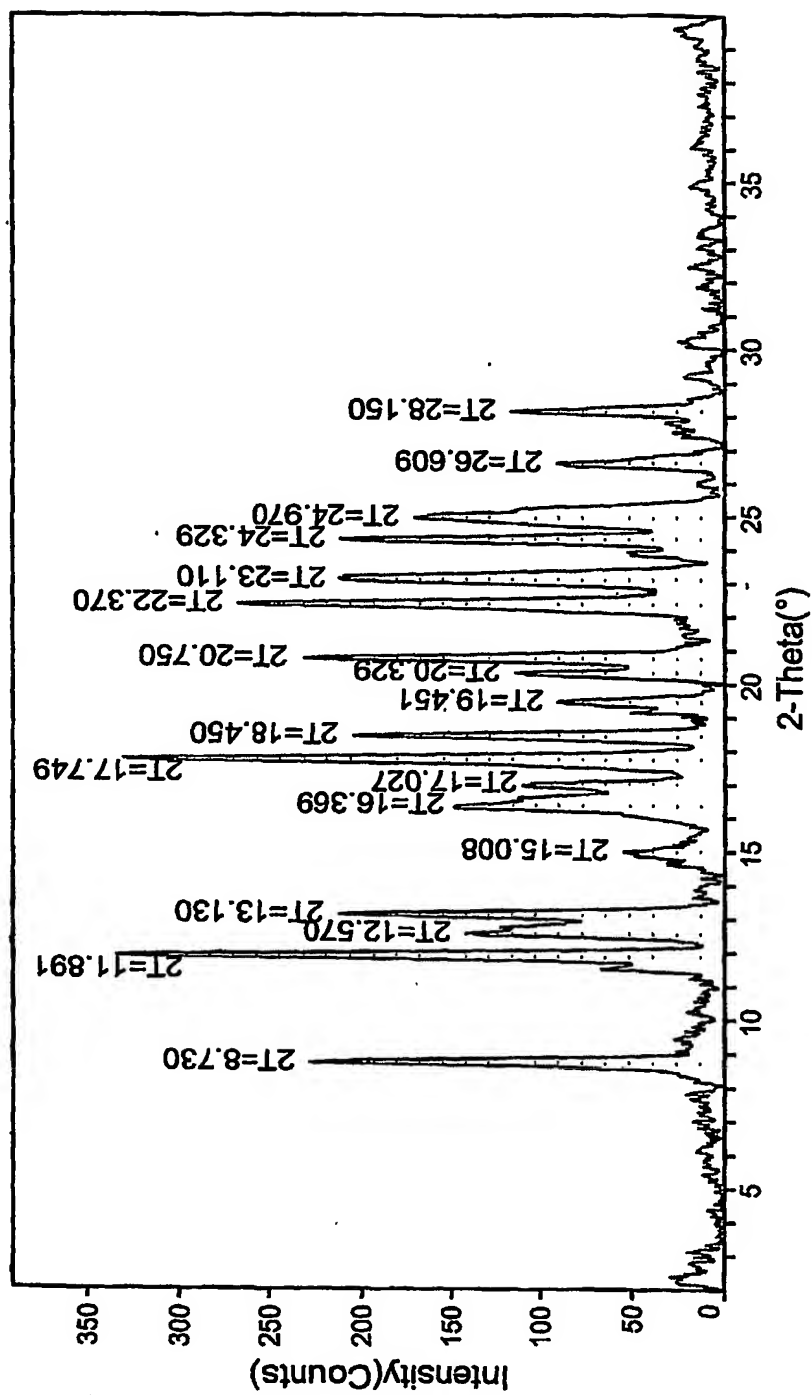


FIG. 86

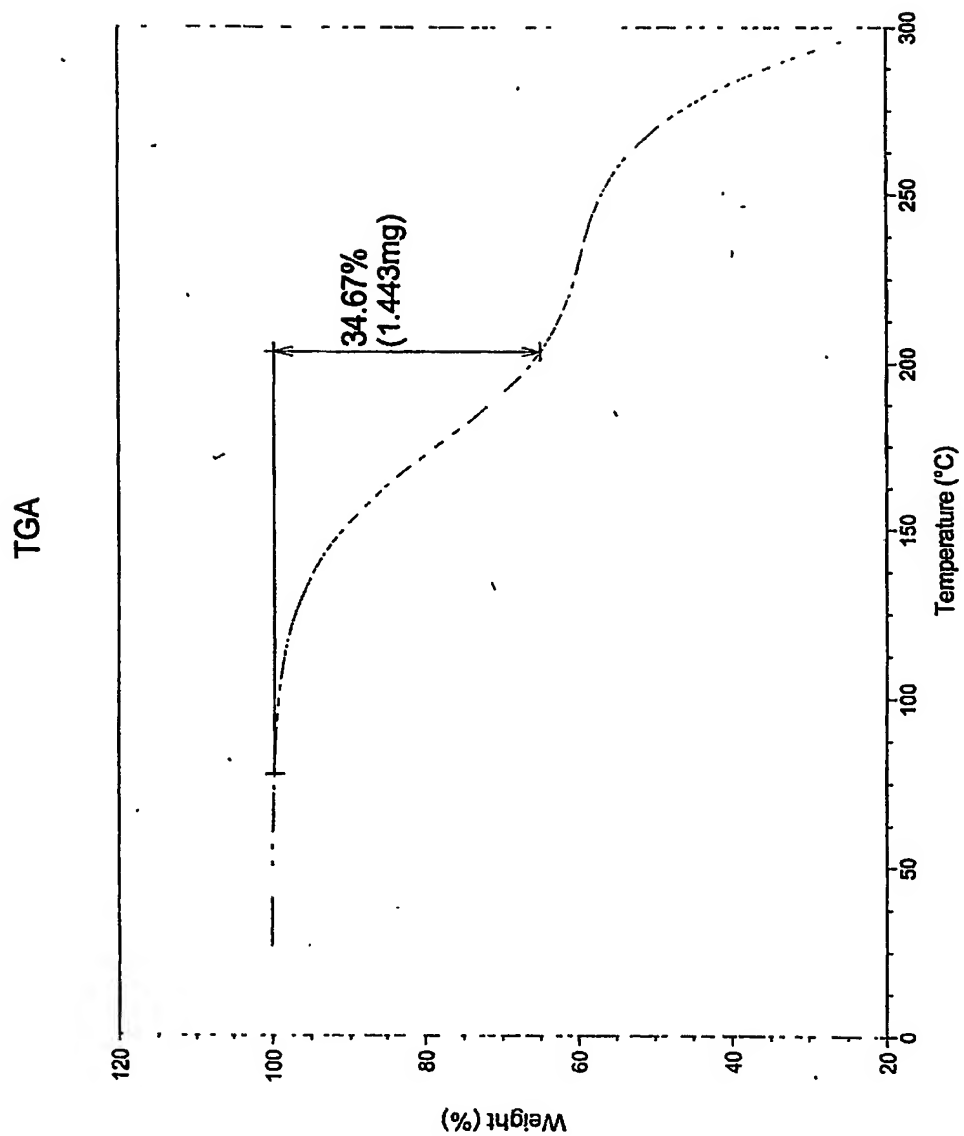


FIG. 87

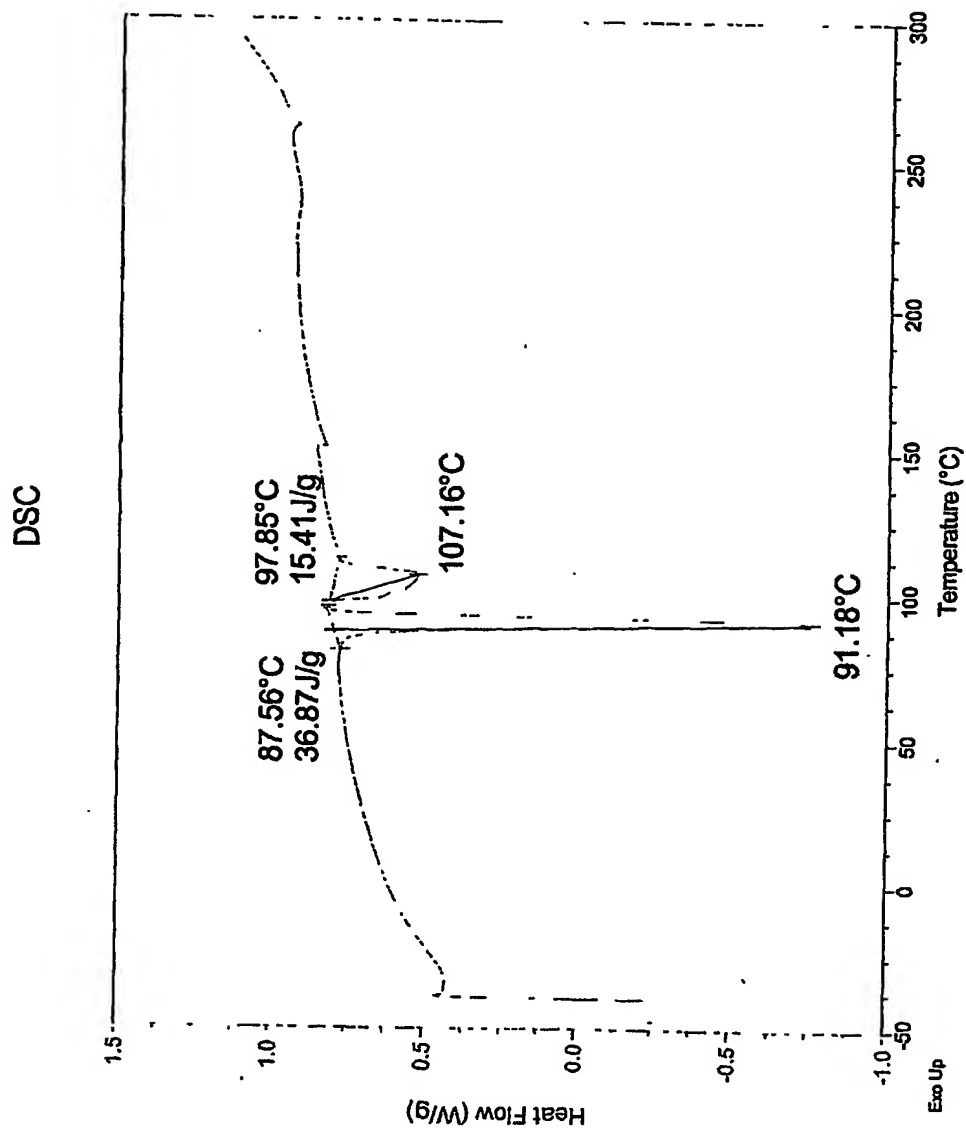


FIG. 88

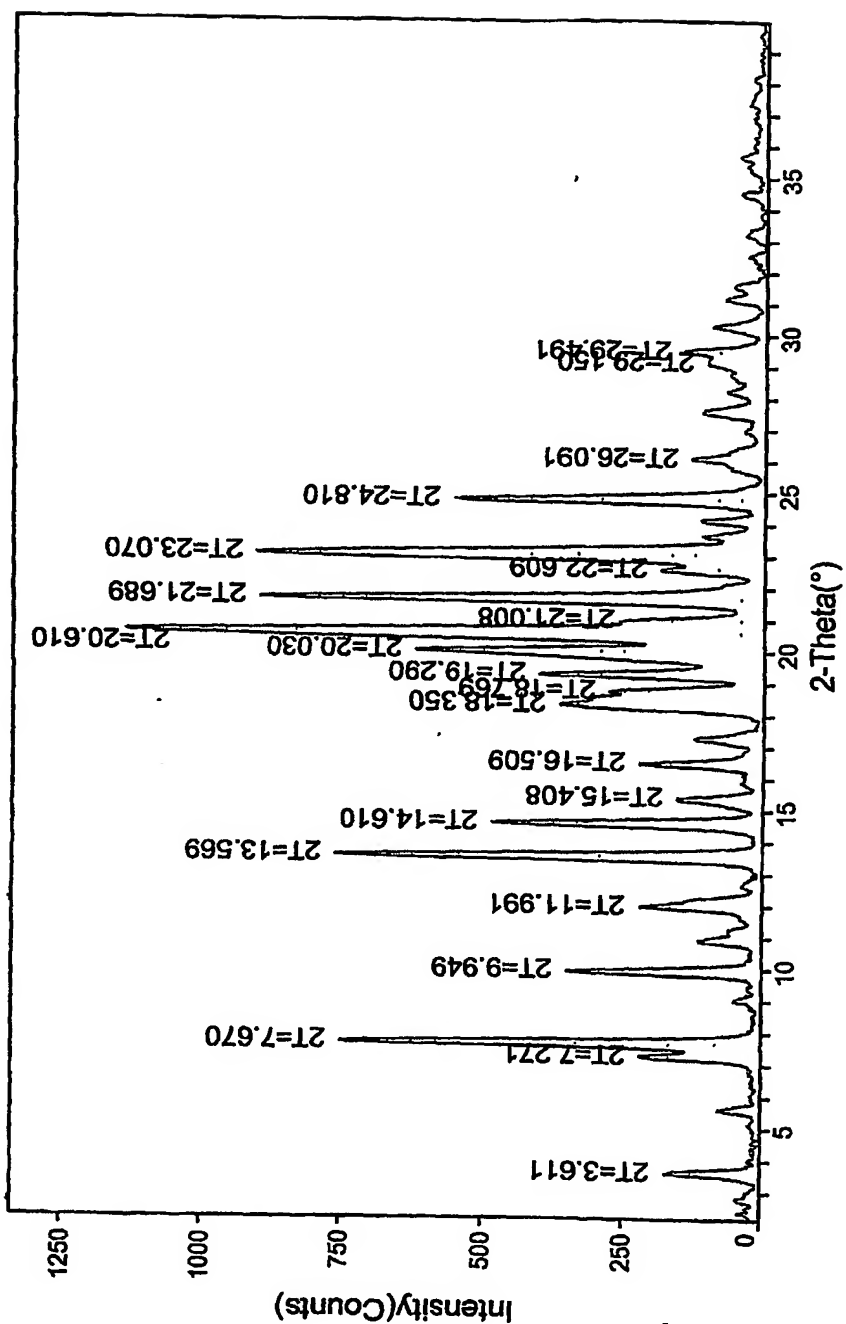


FIG. 89

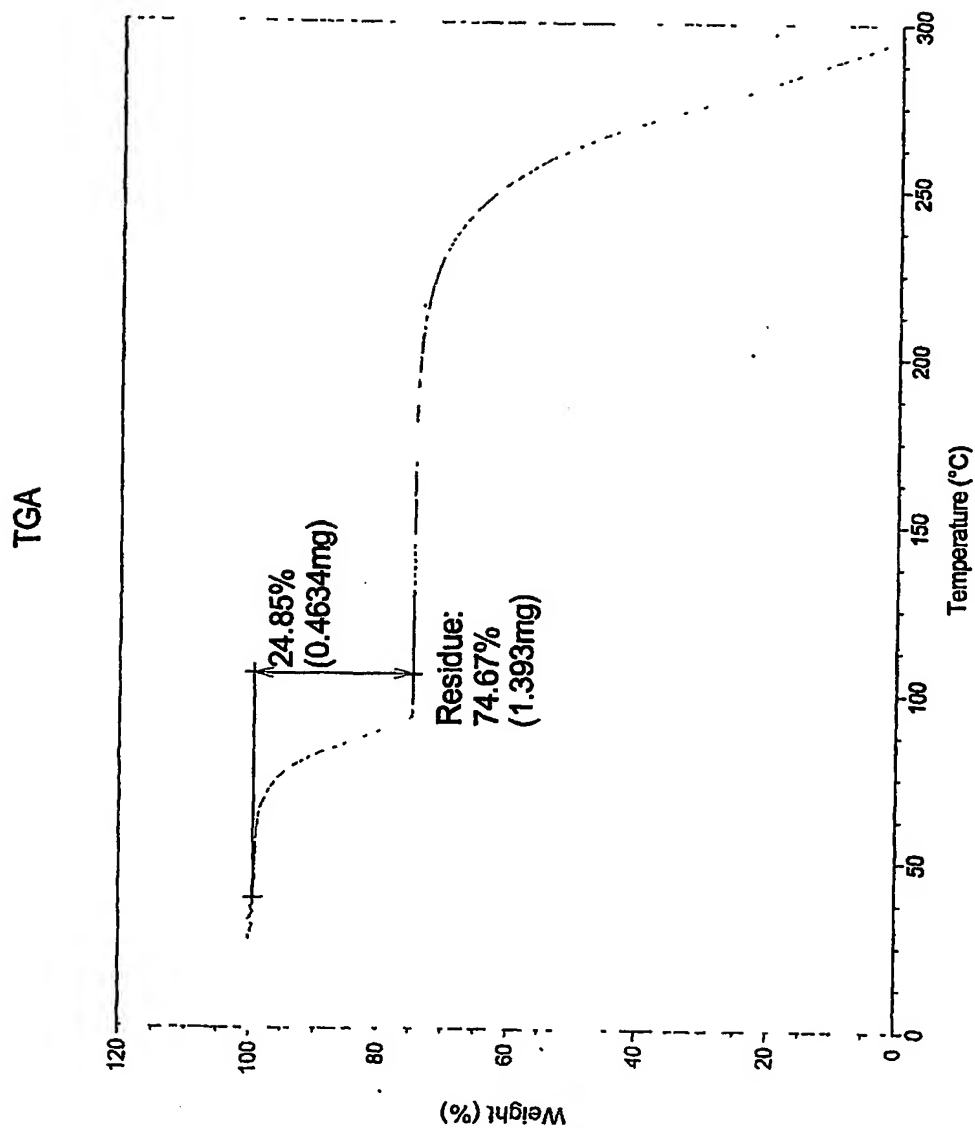


FIG. 90

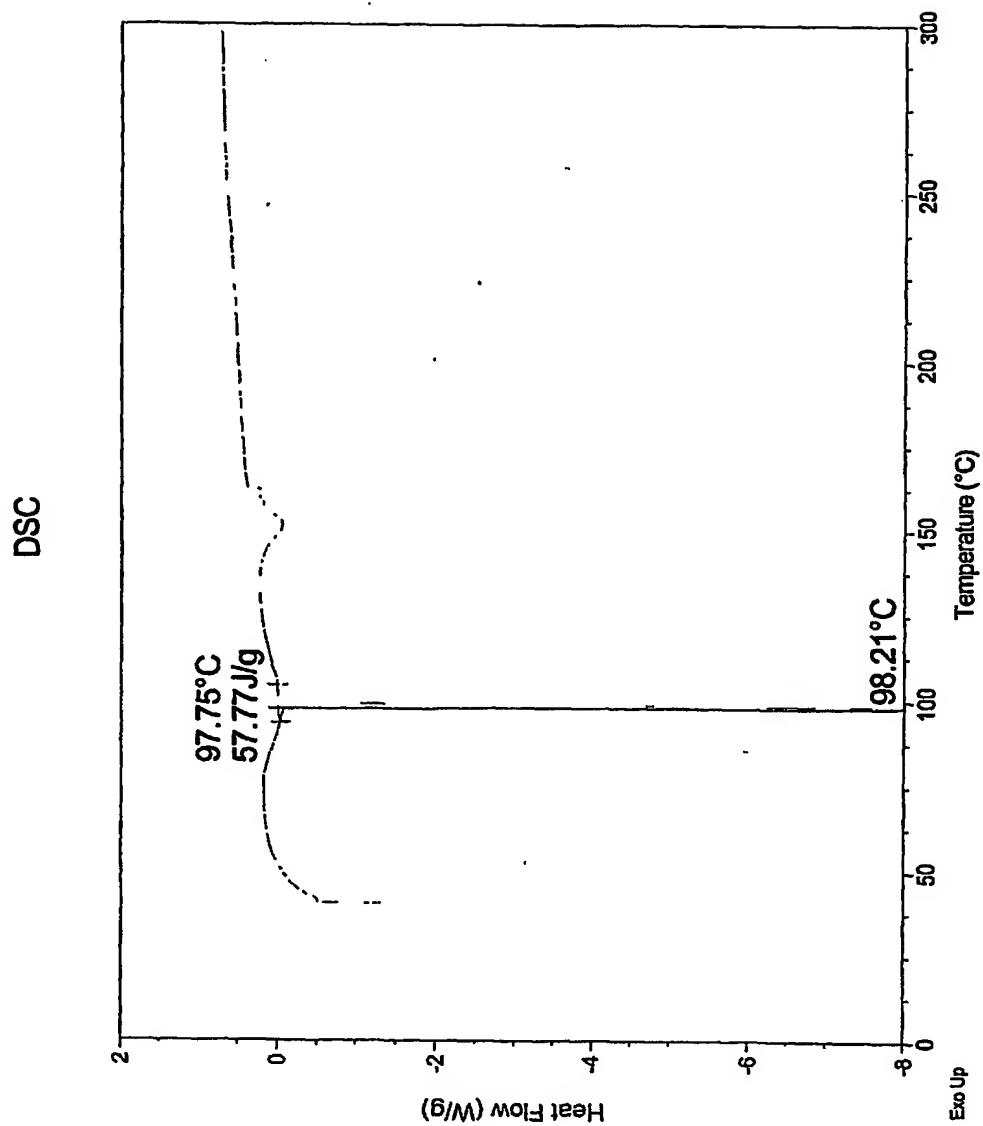


FIG. 91

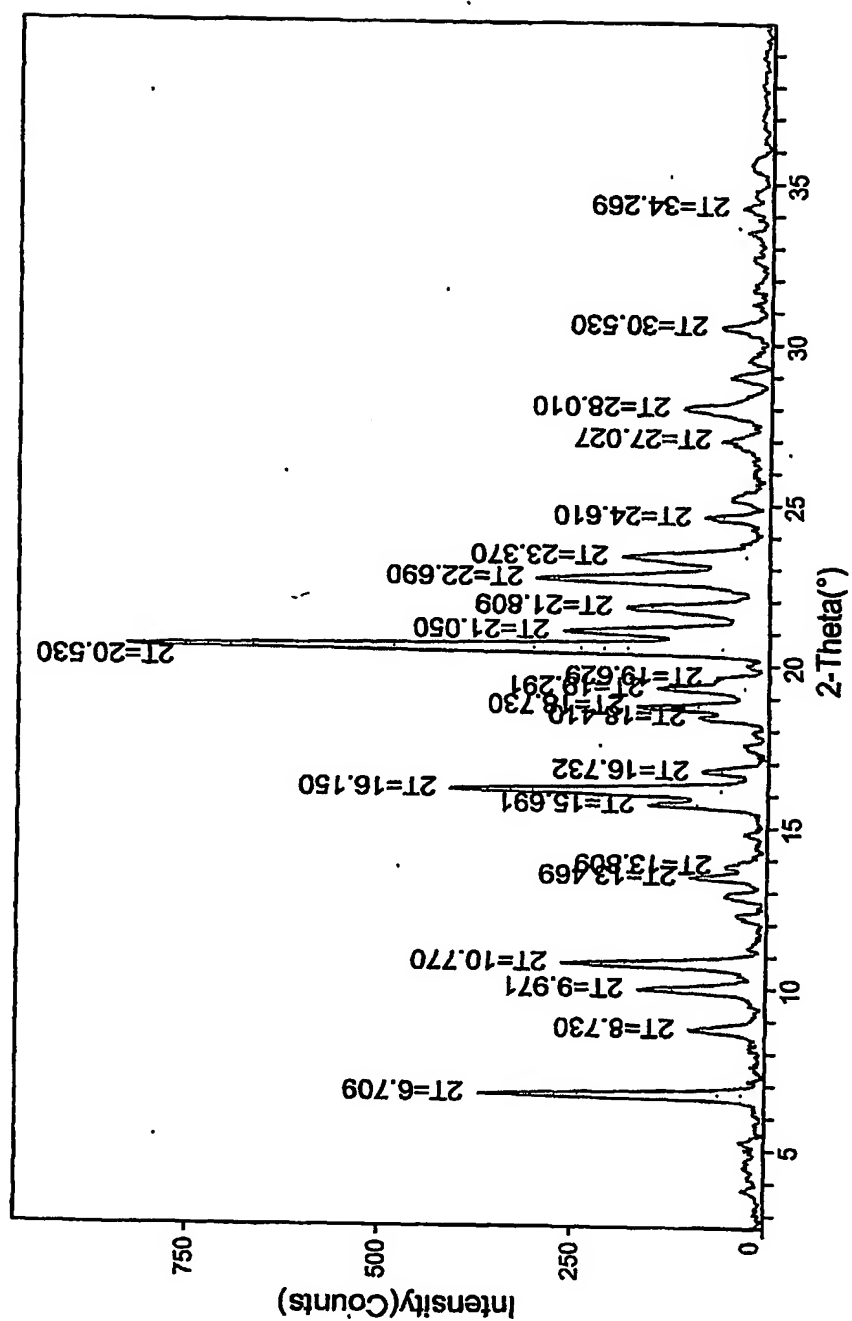


FIG. 92

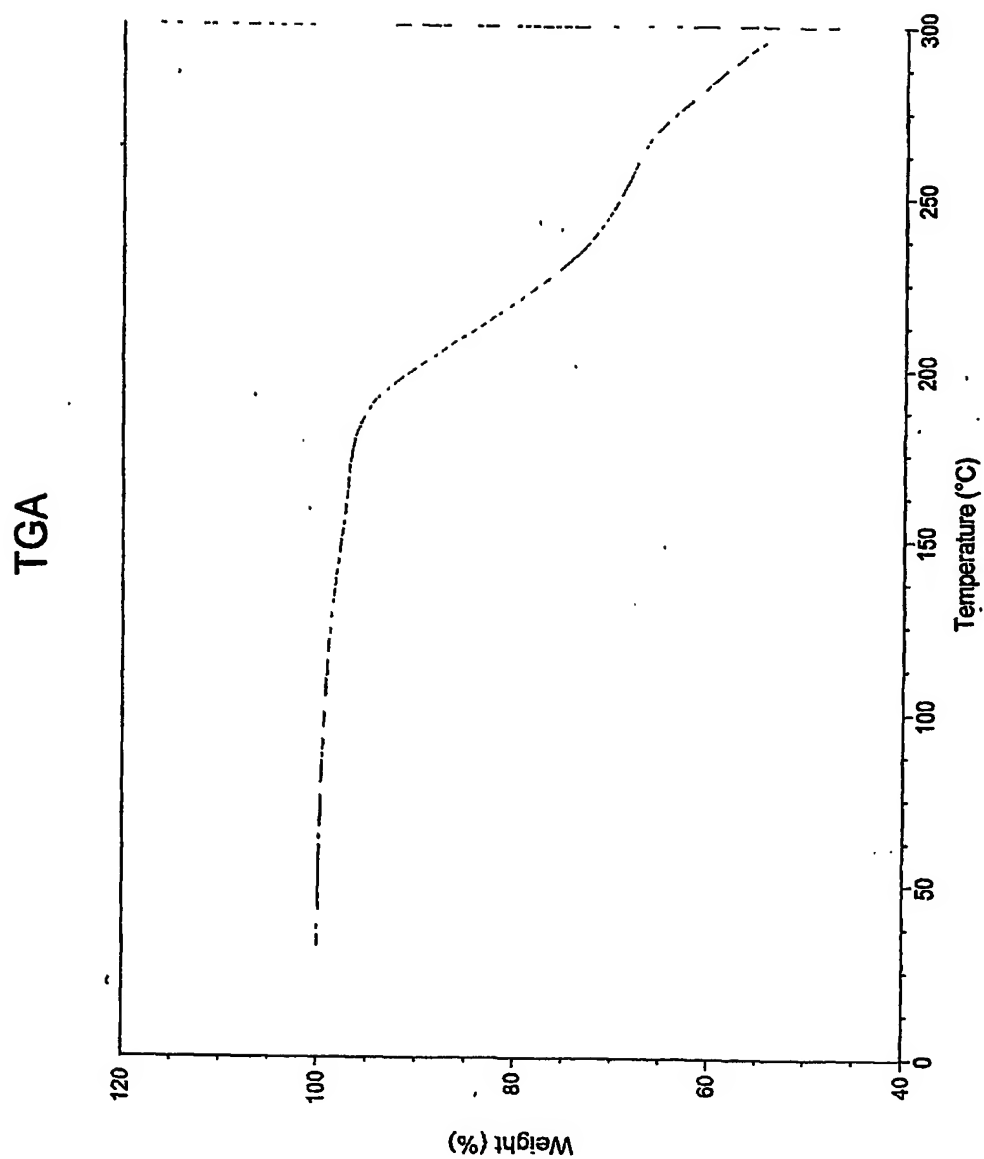


FIG. 93



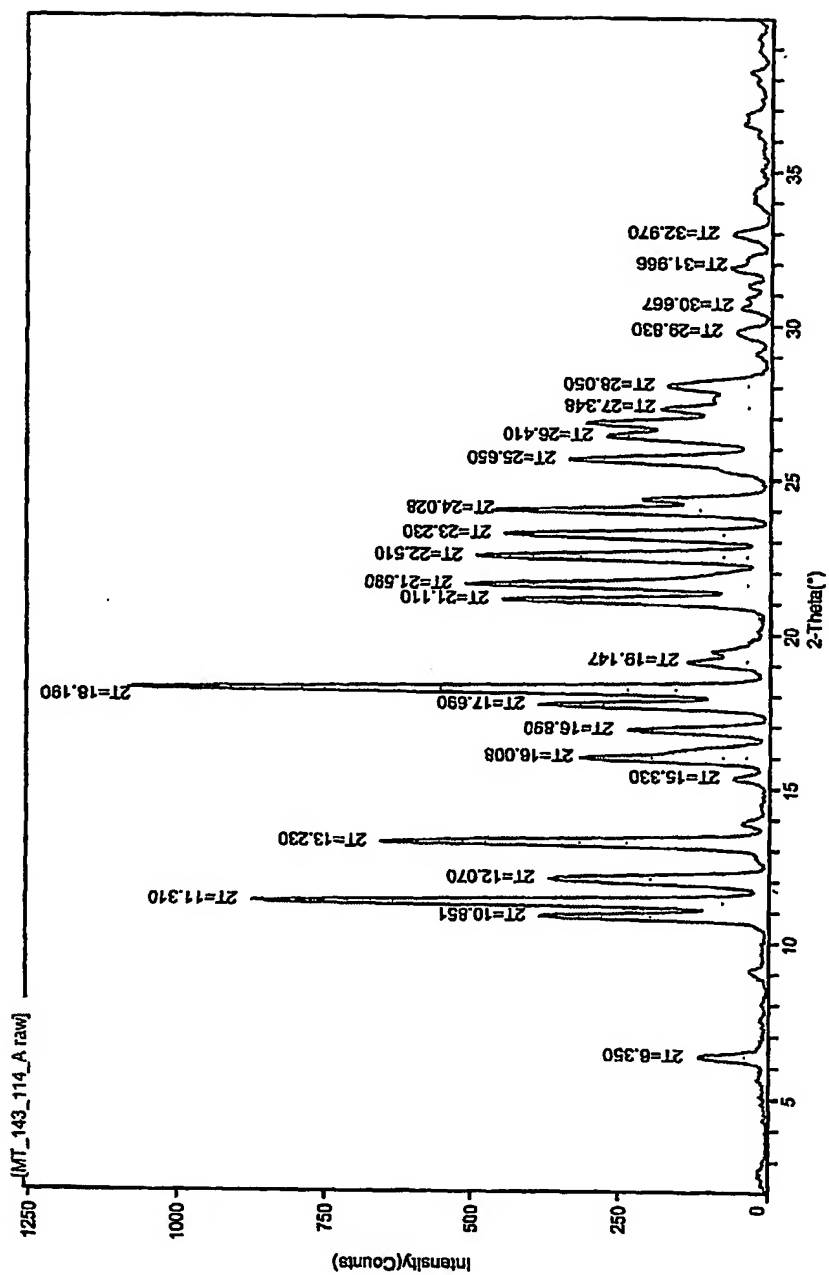


FIG. 94

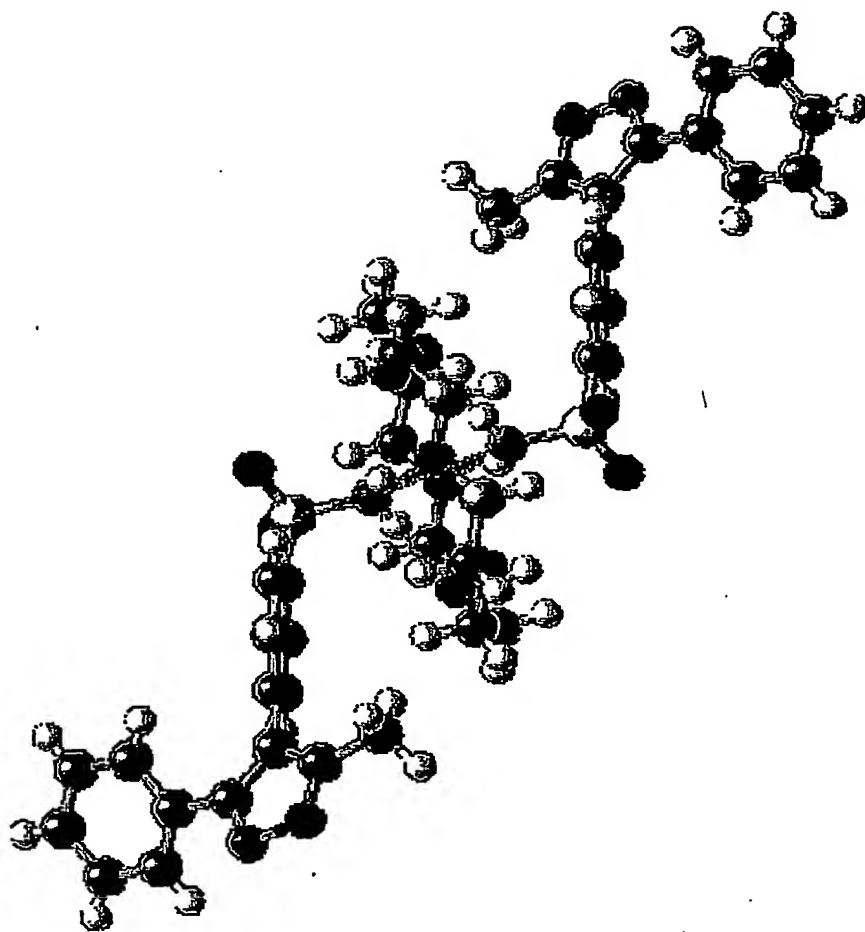


FIG. 95

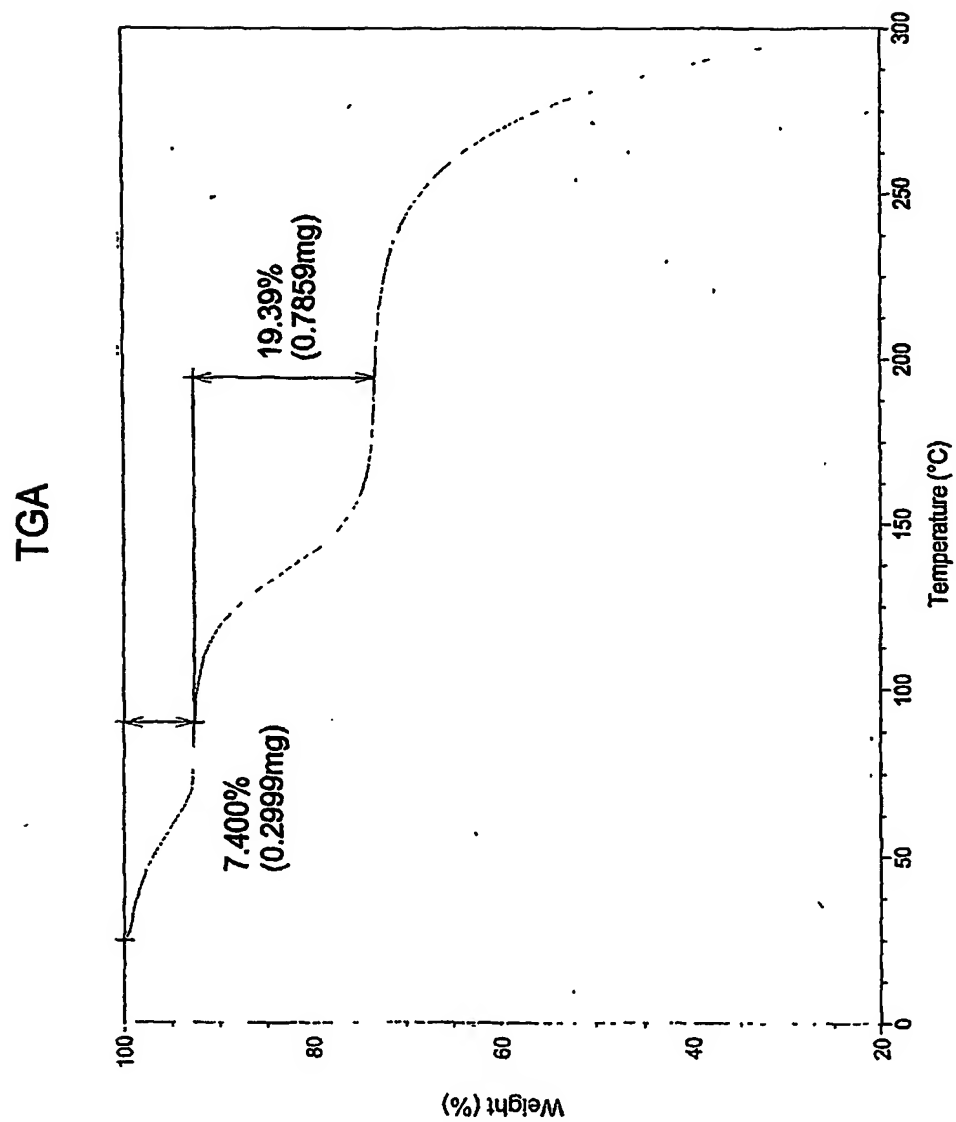


FIG. 96

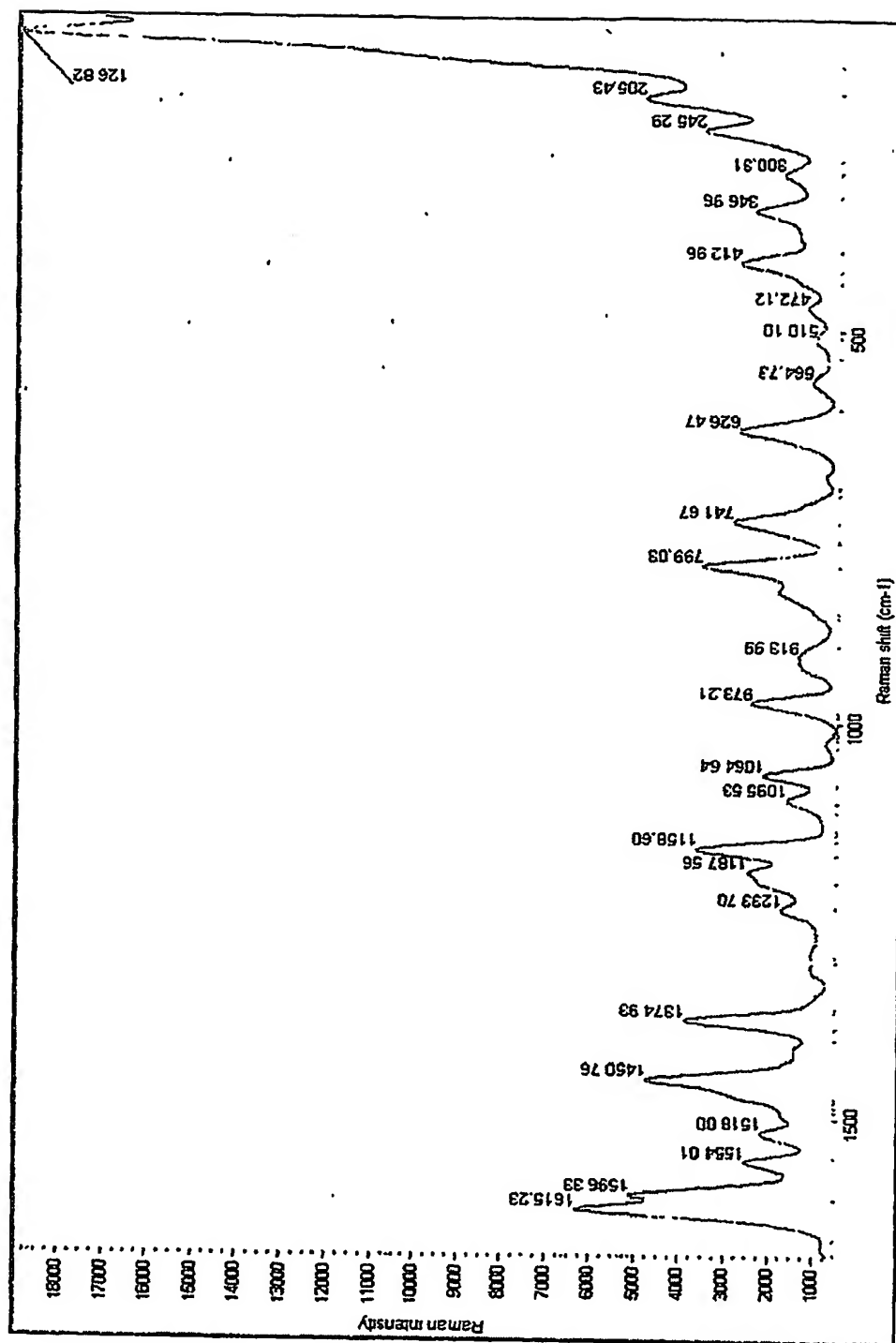


FIG. 97

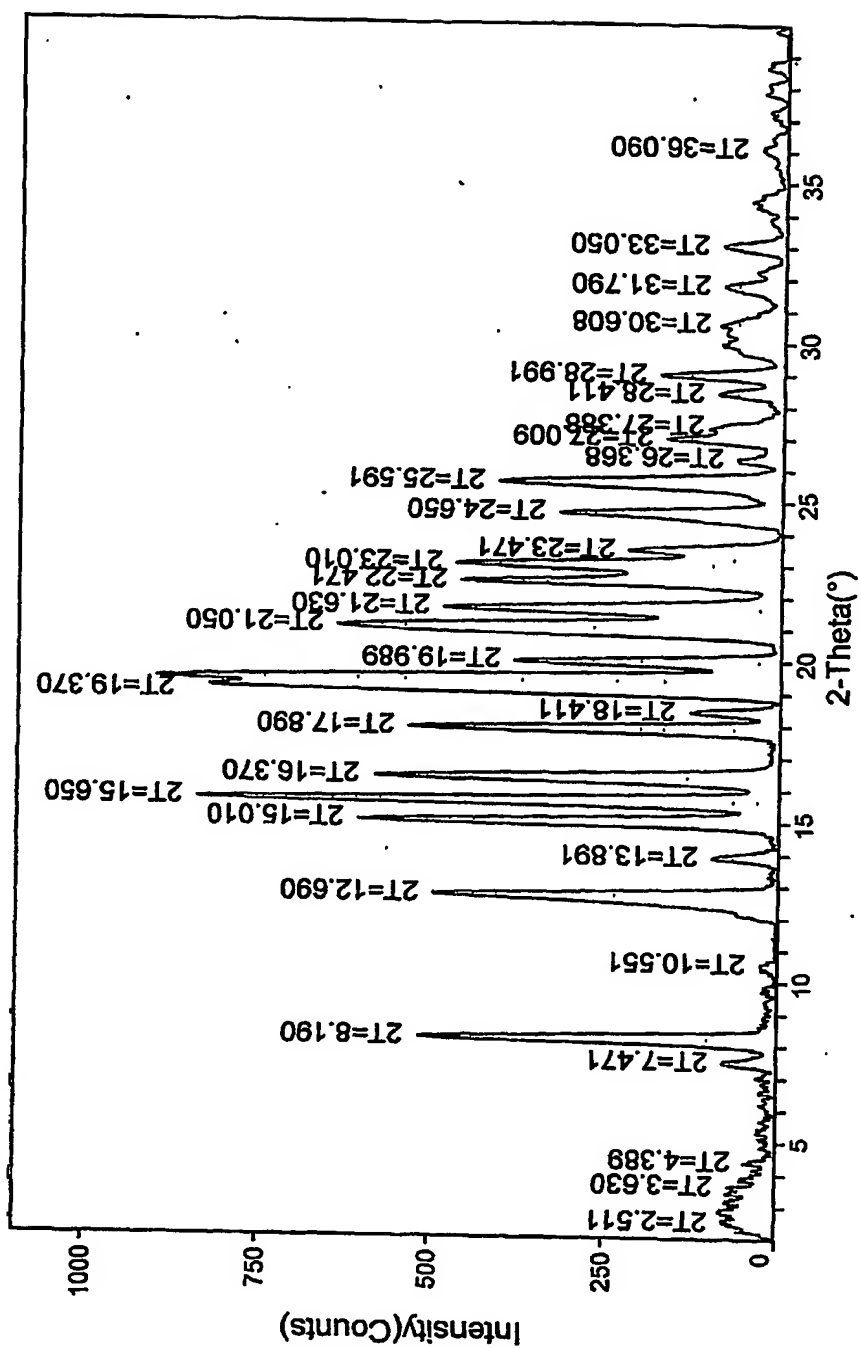


FIG. 98

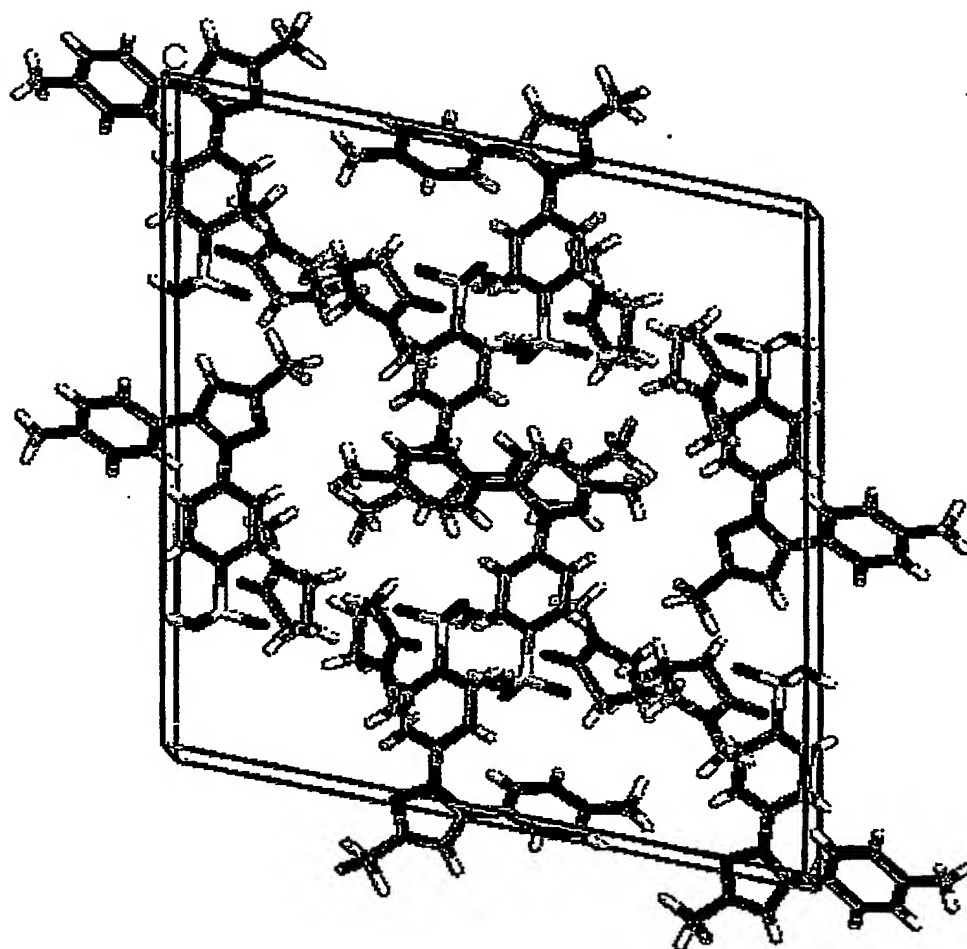


FIG. 99

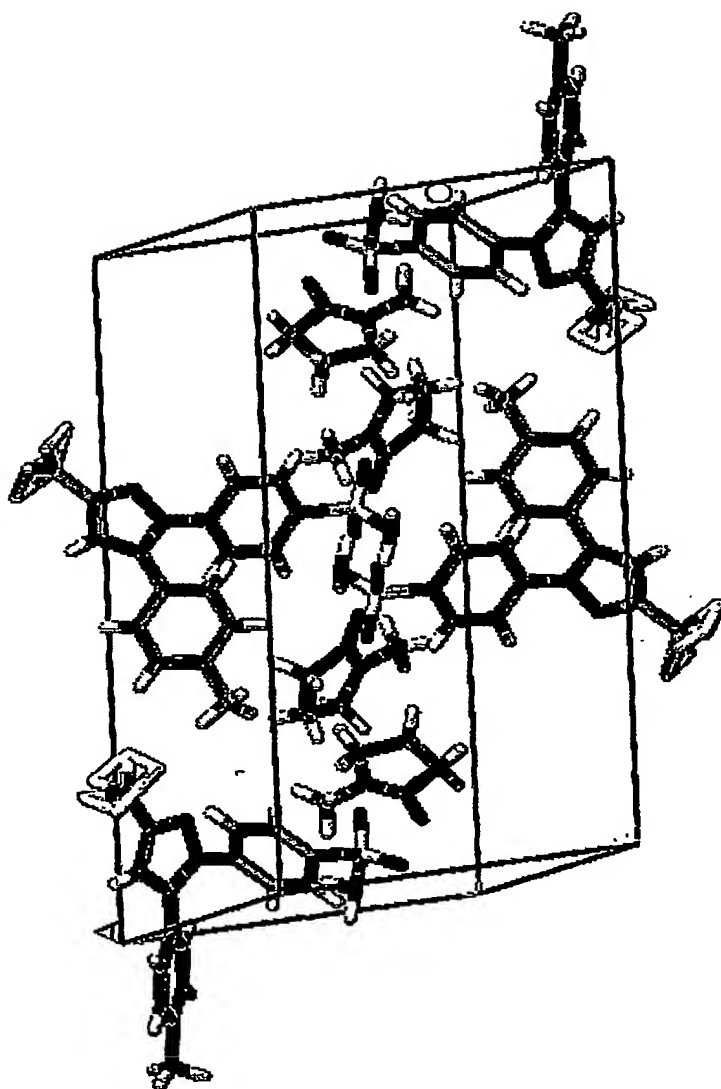


FIG. 100

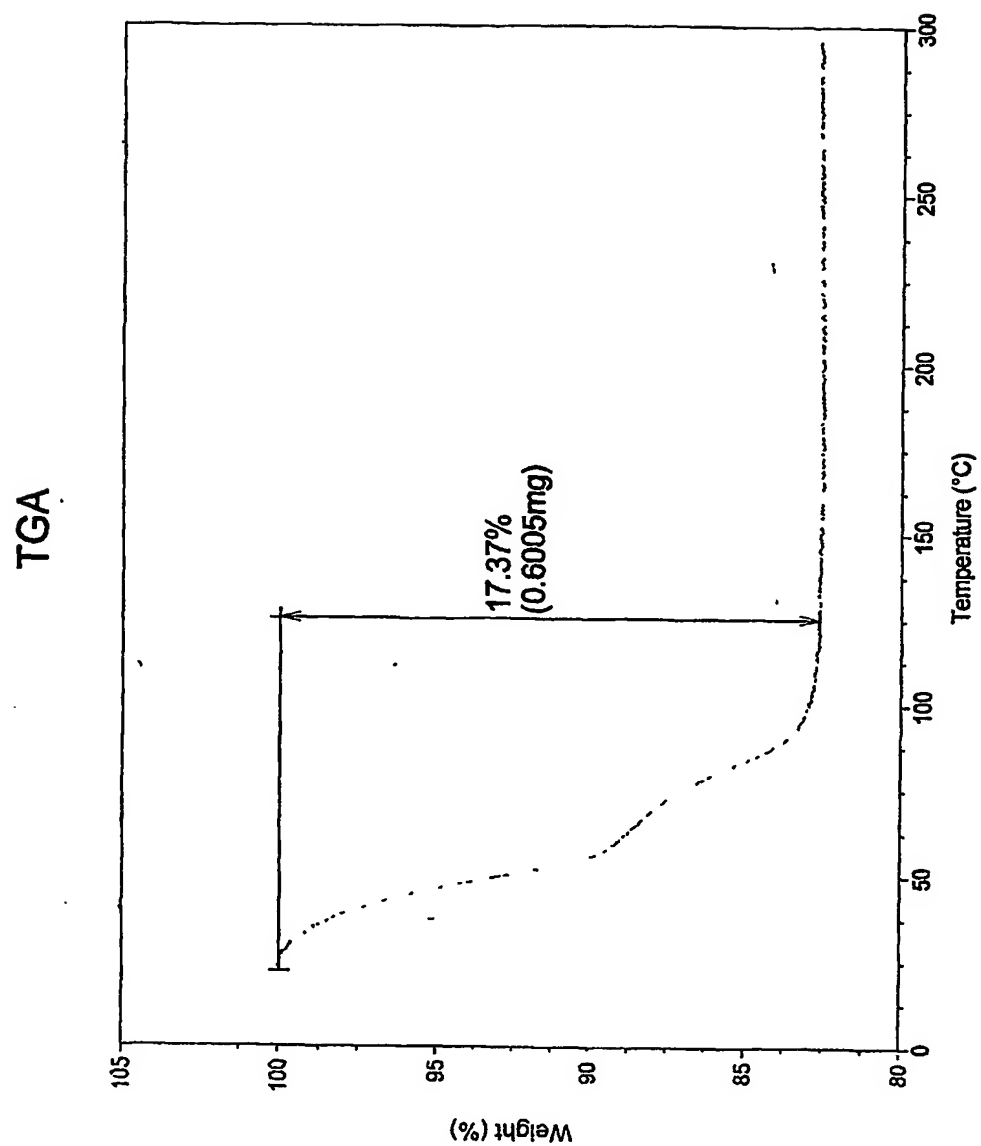


FIG. 101



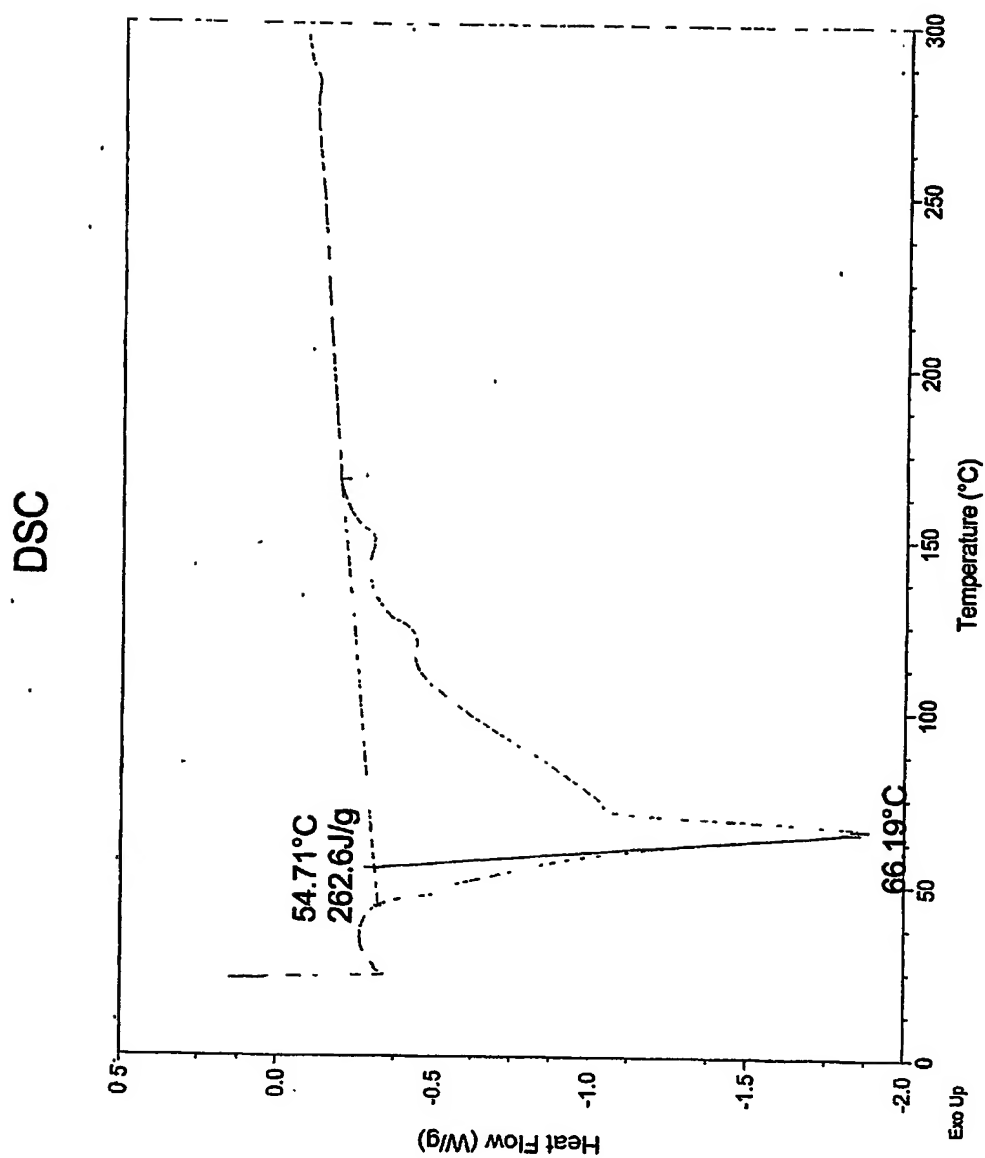


FIG. 102